09/203506
Att #16

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1. Document ID: US 6008014 A
Entry 1 of 88
File: USPT
Dec 28, 1999

US-PAT-NO: 6008014
DOCUMENT-IDENTIFIER: US 6008014 A

TITLE: Method of making lipid metabolic pathway compositions

DATE-ISSUED: December 28, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gimeno; Carlos J.	Boston	MA	N/A	N/A
Acton; Susan	Jamaica Plain	MA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/325, 435/455, 435/91.1, 536/23.1

ABSTRACT:

The present invention relates to the discovery of novel genes encoding Lipid Metabolic Pathway (LMP) polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.
29 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

2. Document ID: US 6004941 A
Entry 2 of 88
File: USPT
Dec 21, 1999

US-PAT-NO: 6004941
DOCUMENT-IDENTIFIER: US 6004941 A

TITLE: Methods for regulating gene expression

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A	N/A

US-CL-CURRENT: 514/44; 424/93.21, 435/320.1, 435/325, 435/455, 435/69.1, 435/70.1, 536/23.4, 536/24.1

ABSTRACT:

Methods of regulating gene expression in subjects using tetracycline-responsive fusion proteins are disclosed. In one embodiment, the method involves introducing into a cell the subject a nucleic acid molecule encoding a fusion protein which activates transcription, the fusion protein comprising a first polypeptide which binds to a tet operator sequence in the presence of tetracycline or a tetracycline analogue operatively linked to a second polypeptide which activates transcription in eukaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject. In another embodiment, the cell further comprises a fusion protein which inhibits transcription, the fusion protein comprising a first polypeptide which binds to a tet operator sequence, operatively linked to a second polypeptide which inhibits transcription in eukaryotic cells. In yet another embodiment, the method involves obtaining a cell from a subject, introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one tet operator sequence, introducing into the cell a second nucleic acid molecule encoding a fusion protein of the invention to form a modified cell, administering the modified cell to the subject and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first and second nucleic acid molecules can be linked or can be separate molecules.
40 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

3. Document ID: US 6001619 A
Entry 3 of 88
File: USPT
Dec 14, 1999

US-PAT-NO: 6001619
DOCUMENT-IDENTIFIER: US 6001619 A

TITLE: Ubiquitin ligases, and uses related thereto

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Beach; David	Huntington Bay	NY	N/A	N/A
Caligiuri; Maureen G.	Huntington	NY	N/A	N/A
Nefsky; Bradley	Highland Park	NJ	N/A	N/A

US-CL-CURRENT: 435/193; 536/23.2

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells of a ubiquitin ligases. These proteins are referred to herein collectively as "pub" proteins for Protein UBiquitin ligase, and individually as h-pub1, h-pub2 and s-pub1 for the human pub1 and pub2 and Schizosaccharomyces pombe pub1 clones, respectively. Pub1 proteins apparently play a role in the ubiquitination of the mitotic activating tyrosine phosphatase cdc25, and thus they may regulate the progression of proliferation in eukaryotic cells by activating the cyclin dependent kinase complexes. In S. pombe, disruption of s-pub1 elevates the level of cdc25 protein in vivo increasing the activity of the tyrosine kinases, wee1 and mik1, required to arrest the cell-cycle. Loss of wee1 function in an S. pombe cell carrying a disruption in the s-pub1 gene results in a lethal premature entry into mitosis; such lethal phenotype can be rescued by the loss of cdc25 function. An ubiquitin thioester adduct of s-pub1 can be isolated from S. pombe and disruption of s-pub1 dramatically reduces ubiquitination of cdc25.

33 Claims, 0 Drawing figures
Exemplary Claim Number: 1

4. Document ID: US 5998174 A
Entry 4 of 88

File: USPT

Dec 7, 1999

US-PAT-NO: 5998174
DOCUMENT-IDENTIFIER: US 5998174 A

TITLE: Multigene vectors

DATE-ISSUED: December 7, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Glorioso; Joseph C.	Cheswick	PA	N/A	N/A
Krisky; David	Pittsburgh	PA	N/A	N/A

US-CL-CURRENT: 435/91.4; 435/320.1, 435/455, 435/463, 435/465, 435/91.41, 435/91.42, 435/91.5, 536/23.7, 536/23.72

ABSTRACT:

The present invention provides a method for preparing HSV vectors. The method comprises co-transfecting a source vector and a mutating cassette together into a population of appropriate host cells, such that homologous recombination occurs between the mutating cassette and the source vector whereby the mutating cassette replaces a region of the HSV genome. The mutating cassette has a unique restriction site not present in the sequence of the vector. The method further comprises plaquing the co-transfected host cells, selecting plaques in which recombination has occurred between the source vector and the mutating cassette, and isolating the viral DNA from the plaques. The isolated viral DNA is digested with a restriction endonuclease appropriate for cleaving the viral DNA at the unique restriction site within the mutating cassette to produce two viral polynucleotides. Following purification, the two viral polynucleotides can be ligated to form an HSV vector comprising the two viral polynucleotides. Alternatively, the two isolated viral polynucleotides can be recombined with an insertion cassette to form an HSV vector comprising the insertion cassette at the former locus of the unique restriction site. The present invention further provides a mutant vector, particularly an HSV vector constructed in accordance with the method for the present invention. The present invention further provides a multigene HSV vector, particularly a multigene HSV vector for cancer therapy.

11 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

5. Document ID: US 5994503 A
Entry 5 of 88

File: USPT

Nov 30, 1999

US-PAT-NO: 5994503
DOCUMENT-IDENTIFIER: US 5994503 A

TITLE: Nucleotide and protein sequences of lats genes and methods based thereon

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Xu; Tian	Guilford	CT	N/A	N/A
Tao; Wufan	Branford	CT	N/A	N/A
Wang; Weiyi	New Haven	CT	N/A	N/A
Zhang; Sheng	New Haven	CT	N/A	N/A
Yu; Wan	Guilford	CT	N/A	N/A

US-CL-CURRENT: 530/350; 435/194, 435/7.1, 435/925, 530/300, 530/324, 530/325, 530/326

ABSTRACT:

The present invention relates to a tumor suppressor gene, termed large tumor suppressor (lats), and methods for identifying tumor suppressor genes. The method provides nucleotide sequences of lats genes, and amino acid sequences of their encoded proteins, as well as derivatives (e.g., fragments) and analogs thereof. In a specific embodiment, the lats protein is a human protein. The invention further relates to fragments (and derivatives and analogs thereof) of lats which comprise one or more domains of a lats protein. Antibodies to lats, its derivatives and analogs, are additionally provided. Methods of production of the lats proteins, derivatives and analogs, e.g., by recombinant means, are also provided. Therapeutic and diagnostic methods and pharmaceutical compositions are provided. The invention also relates to recombinant plants and animals and methods of increasing the growth of edible plants and animals. In specific examples, isolated lats genes, from Drosophila, mouse, and human, and the sequences thereof, are provided.
67 Claims, 15 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 43

6. Document ID: US 5994070 A
Entry 6 of 88
File: USPT
Nov 30, 1999

US-PAT-NO: 5994070
DOCUMENT-IDENTIFIER: US 5994070 A

TITLE: Trio molecules and uses related thereto

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Streuli; Michel	Brookline	MA	N/A	N/A
Debant; Anne	Padres le Lez	N/A	N/A	FRX
Serra-Pages; Carles	Boston	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/325, 435/69.1, 536/23.5, 536/24.31

ABSTRACT:

Nucleic acids encoding TRIO proteins, the TRIO proteins themselves, and active portions thereof as described. In addition, antibodies immunoreactive with TRIO proteins, and preparations of such compositions are provided. Diagnostic and therapeutic assays and reagents for detecting and treating disorders involving, for example, aberrant expression (or loss thereof) of the TRIO protein are described. Assays are provided for identifying agents that modulate the biological function of TRIO proteins.
25 Claims, 50 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 27

7. Document ID: US 5989804 A
Entry 7 of 88
File: USPT
Nov 23, 1999

US-PAT-NO: 5989804
DOCUMENT-IDENTIFIER: US 5989804 A

TITLE: E6 binding proteins

DATE-ISSUED: November 23, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Androphy; Elliot J.	Natick	MA	N/A	N/A
Chen; Jason J.	Boston	MA	N/A	N/A

US-CL-CURRENT: 435/5; 435/7.23, 435/7.6, 435/7.7, 435/7.71, 435/7.72, 435/7.92, 514/12, 530/300, 530/350, 536/23.5, 536/23.72, 930/220

ABSTRACT:

E6-BP polypeptides, nucleic acids encoding E6-BP polypeptides, and uses thereof.
10 Claims, 3 Drawing figures
Exemplary Claim Number: 1,7
Number of Drawing Sheets: 3

8. Document ID: US 5986054 A
Entry 8 of 88
File: USPT
Nov 16, 1999

US-PAT-NO: 5986054
DOCUMENT-IDENTIFIER: US 5986054 A

TITLE: Genetic sequences and proteins related to alzheimer's disease

DATE-ISSUED: November 16, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
St. George-Hyslop; Peter H.				

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Rommens; Johanna M.
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US-CL-CURRENT: 530/350; 435/69.1

ABSTRACT:

The present invention describes the identification, isolation and cloning of two human presenilin genes, PS-1 and PS-2, mutations in which lead to Familial Alzheimer's Disease. Also identified are presenilin homologue genes in mice, C. elegans and D. melanogaster. Transcripts and products of these genes are useful in detecting and diagnosing Alzheimer's disease, developing therapeutics for treatment of Alzheimer's disease, as well as the isolation and manufacture of the protein and the constructions of transgenic animals expressing the mutant genes.
29 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 12

9. Document ID: US 5981702 A
Entry 9 of 88
File: USPT
Nov 9, 1999

US-PAT-NO: 5981702
DOCUMENT-IDENTIFIER: US 5981702 A

TITLE: Cyclin/CDK associated proteins, and uses related thereto

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:
NAME
CITY
STATE
ZIP CODE
COUNTRY
Zhang; Hui
Huntington Station
NY
N/A
N/A
Beach; David
Huntington Bay
NY
N/A
N/A

US-CL-CURRENT: 530/350

ABSTRACT:

The present invention relates to the discovery in mammalian cells, particularly human cells, of novel S-phase kinase associated proteins, p19 and p45, referred to herein as "Skp". As described herein, these proteins are components of the tumor cell-specific cyclin A/CDK2 complex and function to facilitate DNA replication. Interference with p45 function in vivo prevented entry into S-phase in both normal and transformed cells. Binding data indicated that p45 and p19 associate with each other in a binary complex. Moreover, p45 is required for p19 binding to cyclin A/CDK2.
13 Claims, 0 Drawing figures
Exemplary Claim Number: 1

10. Document ID: US 5968821 A
Entry 10 of 88
File: USPT
Oct 19, 1999

US-PAT-NO: 5968821
DOCUMENT-IDENTIFIER: US 5968821 A

TITLE: Cell-cycle regulatory proteins, and uses related thereto

DATE-ISSUED: October 19, 1999

INVENTOR-INFORMATION:
NAME
CITY
STATE
ZIP CODE
COUNTRY
Beach; David H.
Huntington Bay
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N/A
Demetrick; Douglas J.
E. Northport
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Serrano; Manuel
Mill Neck
NY
N/A
N/A
Hannon; Gregory J.
Huntington
NY
N/A
N/A

US-CL-CURRENT: 435/325; 435/320.1, 435/455, 435/6, 435/69.1, 536/23.1

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of a novel family of cell-cycle regulatory proteins ("CCR-proteins"). As described herein, this family of proteins includes a polypeptide having an apparent molecular weight of 16 kDa, and a polypeptide having an apparent molecular weight of approximately 15 kDa, each of which can function as an inhibitor of cell-cycle progression, and therefore ultimately of cell growth.
Thus, similar to the role of p21 to the p53 checkpoint, the subject CCR-proteins may function coordinately with the cell-cycle regulatory protein, retinoblastoma (RB). Furthermore, the CCR-protein family includes a protein having an apparent molecular weight of 13.5 kDa (hereinafter "p13.5"). The presumptive role of p13.5, like p16 and p15, is in the regulation of the cell-cycle.

35 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

11. Document ID: US 5965791 A
Entry 11 of 88
File: USPT
Oct 12, 1999

US-PAT-NO: 5965791
DOCUMENT-IDENTIFIER: US 5965791 A

TITLE: Vector for introducing a gene into a plant, and methods for producing transgenic plants
and multitudinously introducing genes into a plant using the vector

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ebinuma; Hiroyasu	Tokyo	N/A	N/A	JPX
Sugita; Koichi	Tokyo	N/A	N/A	JPX
Matsunaga; Etsuko	Tokyo	N/A	N/A	JPX
Yamakado; Mikiko	Tokyo	N/A	N/A	JPX

ABSTRACT:

A vector for introducing a desired gene into a planet, which comprises the desired gene and at least one morphological abnormally
induction (MAI) gene as a marker gene, or which comprises the desired gene, at least one MAI gene and a removable element. A
method for producing a transgenic plant free from the influence of a marker gene. A method for multitudinously introducing desired
genes into one plant.
30 Claims, 29 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 29

12. Document ID: US 5965790 A
Entry 12 of 88
File: USPT
Oct 12, 1999

US-PAT-NO: 5965790
DOCUMENT-IDENTIFIER: US 5965790 A

TITLE: SR-BI regulatory sequences and therapeutic methods of use

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Acton; Susan Laurene	Lexington	MA	N/A	N/A

US-CL-CURRENT: 800/18; 435/29, 435/320.1, 435/325, 435/6, 536/24.1, 536/24.31, 800/21

ABSTRACT:

The invention features nucleic acid molecules that are involved with (e.g. activate or regulate)
human SR-BI receptor transcription, as well as complements thereto, and homologs thereof. In
addition, drug discovery assays are provided for identifying agents which modulate SR-BI promoter
activity and thereby modulate the expression of a gene regulated thereby. Such agents can be
useful therapeutically for treating or preventing the development of a disease or condition that
is caused or contributed to by an aberrant SR-BI activity. In a preferred embodiment, the disease
or condition is characterized by inappropriate lipid transfer or metabolism (e.g.,
atherosclerosis or gallstone formation). Such agents can also be used to modulate expression of a
specific gene under the control of the SR-BI promoter in gene therapy. Moreover, the present
invention provides diagnostic assays and reagents for determining whether a subject has a
disorder involving, for example, aberrant expression of SR-BI genes.
31 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

13. Document ID: US 5962316 A
Entry 13 of 88
File: USPT
Oct 5, 1999

US-PAT-NO: 5962316
DOCUMENT-IDENTIFIER: US 5962316 A

TITLE: Cell-cycle regulatory proteins, and uses related thereto

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Beach; David H.	Huntington Bay	NY	N/A	N/A
Demetrick; Douglas J.	Northport	NY	N/A	N/A
Serrano; Manuel	Mill Neck	NY	N/A	N/A

Hannon; Gregory J.
Huntington
NY
N/A
N/A

US-CL-CURRENT: 435/325; 424/185.1, 424/93.21, 435/320.1, 435/455, 435/6, 435/69.1, 514/44, 530/350, 536/23.1, 536/23.4, 536/23.5, 536/24.1

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of a novel family of cell-cycle regulatory proteins ("CCR-proteins"). As described herein, this family of proteins includes a polypeptide having an apparent molecular weight of 16 kDa, and a polypeptide having an apparent molecular weight of approximately 15 kDa, each of which can function as an inhibitor of cell-cycle progression, and therefore ultimately of cell growth. Thus, similar to the role of p21 to the p53 checkpoint, the subject CCR-proteins may function coordinately with the cell-cycle regulatory protein, retinoblastoma (RB). Furthermore, the CCR-protein family includes a protein having an apparent molecular weight of 13.5 kDa (hereinafter "p13.5"). The presumptive role of p13.5, like p16 and p15, is in the regulation of the cell-cycle.
40 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

14. Document ID: US 5955306 A
Entry 14 of 88
File: USPT
Sep 21, 1999

US-PAT-NO: 5955306
DOCUMENT-IDENTIFIER: US 5955306 A

TITLE: Genes encoding proteins that interact with the tub protein

DATE-ISSUED: September 21, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY
Gimeno; Carlos J. | Wellesley | MA | N/A | N/A
Errada; Patrick R. | Cambridge | MA | N/A | N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 435/71.1, 536/23.5, 536/24.3, 536/24.31

ABSTRACT:

The present invention relates to the discovery of novel genes encoding Tub interactor (TI) polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.
23 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

15. Document ID: US 5948653 A
Entry 15 of 88
File: USPT
Sep 7, 1999

US-PAT-NO: 5948653
DOCUMENT-IDENTIFIER: US 5948653 A

TITLE: Sequence alterations using homologous recombination

DATE-ISSUED: September 7, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY
Pati; Sushma | Redwood City | CA | 94061 | N/A
Zarling; David A. | Menlo Park | CA | 94025 | N/A

US-CL-CURRENT: 435/6; 435/470, 435/471, 435/490, 435/91.1, 435/DIG37, 435/DIG5, 435/DIG6, 435/DIG8, 530/350, 536/23.1

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a target cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active target cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active target cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.
40 Claims, 43 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 24

16. Document ID: US 5945339 A
Entry 16 of 88
File: USPT

Aug 31, 1999

US-PAT-NO: 5945339
DOCUMENT-IDENTIFIER: US 5945339 A

TITLE: Methods to promote homologous recombination in eukaryotic cells and organisms

DATE-ISSUED: August 31, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Holloman; William K.	Yorktown Heights	NY	N/A	N/A
Kmiec; Eric B.	Malvern	PA	N/A	N/A

US-CL-CURRENT: 435/477; 435/483, 435/484

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to promote homologous recombination in eukaryotic cells. The application teaches methods by which a recombinase of one species can be used to isolate a homologous recombinase of a different species and methods to identify the isolated homologs. Recombinases from Ustilago maydis, Saccharomyces cerevisiae and humans are specifically included in the invention.

The invention encompasses the method of producing an isolated recombinase protein in a prokaryotic cell and recovering the product in an active form. The invention also encompasses a genetically engineered gene which encodes a non-naturally occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. The invention further encompasses the use of recombinase proteins and of recombinase genes to promote homologous recombination, including recombination between a host cell genome and a chimeric oligonucleotide, i.e., an oligonucleotide having both RNA and DNA bases.
6 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

17. Document ID: US 5925558 A
Entry 17 of 88
File: USPT
Jul 20, 1999

US-PAT-NO: 5925558
DOCUMENT-IDENTIFIER: US 5925558 A

TITLE: Assays for protein kinases using fluorescent protein substrates

DATE-ISSUED: July 20, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsien; Roger Y.	La Jolla	CA	N/A	N/A
Cubitt; Andrew B.	San Diego	CA	N/A	N/A

US-CL-CURRENT: 435/252.3; 435/320.1, 435/325, 435/440, 536/23.1, 536/23.4

ABSTRACT:

This invention provides assays for protein kinase activity using fluorescent proteins engineered to include sequences that can be phosphorylated by protein kinases. The proteins exhibit different fluorescent properties in the non-phosphorylated and phosphorylated states.
23 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 14

18. Document ID: US 5922927 A
Entry 18 of 88
File: USPT
Jul 13, 1999

US-PAT-NO: 5922927
DOCUMENT-IDENTIFIER: US 5922927 A

TITLE: Methods for producing tetracycline-regulated transgenic mice

DATE-ISSUED: July 13, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	Heidelberg	N/A	N/A	DEX
Salfeld; Jochen G.	North Grafton	MA	N/A	N/A
Voss; Jeffrey W.	Framingham	MA	N/A	N/A

US-CL-CURRENT: 800/25; 435/320.1, 435/325, 435/455, 435/463, 435/69.1, 800/18, 800/22

ABSTRACT:

Transgenic mice carrying two transgenes, the first coding for a

transactivator fusion protein
comprising a tet repressor and a polypeptide which directly or indirectly activates in eucaryotic
cells, and the second comprising a gene operably linked to a minimal promoter operably linked to
at least one tet operator sequence, are disclosed. Isolated DNA molecules (e.g., targeting
vectors) for integrating a polynucleotide sequence encoding a transactivator of the invention at
a predetermined location within a second target DNA molecule by homologous recombination are also
disclosed. Transgenic mice having the DNA molecules of the invention integrated at a
predetermined location in a chromosome by homologous recombination are also encompassed by the
invention. Methods to regulate the expression of a tet operator linked-gene of interest by
administering tetracycline or a tetracycline analogue to a mouse of the invention are also
disclosed. The regulatory system of the invention allows for conditional inactivation or
modulation of expression of a gene of interest in a host cell or mouse.
11 Claims, 3 Drawing figures
Exemplary Claim Number: 1,2
Number of Drawing Sheets: 32

19. Document ID: US 5919997 A
Entry 19 of 88
File: USPT
Jul 6, 1999

US-PAT-NO: 5919997
DOCUMENT-IDENTIFIER: US 5919997 A

TITLE: Transgenic mice having modified cell-cycle regulation

DATE-ISSUED: July 6, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Beach; David H.	Huntington Bay	NY	N/A	N/A
Serrano; Manuel	Mill Neck	NY	N/A	N/A
DePinho; Ronald A.	Pelham Manor	NY	N/A	N/A

US-CL-CURRENT: 800/18; 424/9.2, 435/320.1, 435/325, 435/455, 435/463, 435/467, 435/91.2, 800/22, 800/25, 800/3

ABSTRACT:

The present invention relates to transgenic mice in which the biological function of at least one
cell cycle regulatory proteins of the INK4 family is altered.
11 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2

20. Document ID: US 5912411 A
Entry 20 of 88
File: USPT
Jun 15, 1999

US-PAT-NO: 5912411
DOCUMENT-IDENTIFIER: US 5912411 A

TITLE: Mice transgenic for a tetracycline-inducible transcriptional activator

DATE-ISSUED: June 15, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A	N/A

US-CL-CURRENT: 800/18; 435/325, 435/462, 435/463, 435/69.1, 435/70.1, 514/152, 536/23.4, 536/24.1

ABSTRACT:

Transgenic mice carrying a transgene comprising a nucleic acid molecule encoding protein useful
for regulating the expression of genes in eukaryotic cells in a highly controlled manner are
disclosed. In the regulatory system of the invention, transcription of a tet operator-linked
nucleotide sequence is stimulated by a transcriptional activator fusion protein composed of two
polypeptides, a first polypeptide which binds to tet operator sequences in the presence of
tetracycline operatively linked to a second polypeptide activates transcription in eukaryotic
cells. In a preferred embodiment, the transgene encoding the transcriptional activator fusion
protein is integrated at a predetermined location within the chromosome of the transgenic mouse.
36 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

21. Document ID: US 5912326 A
Entry 21 of 88
File: USPT
Jun 15, 1999

US-PAT-NO: 5912326
DOCUMENT-IDENTIFIER: US 5912326 A

TITLE: Cerebellum-derived growth factors

DATE-ISSUED: June 15, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY

Chang; Han
Mountain View
CA
N/A
N/A

US-CL-CURRENT: 530/399; 530/350

ABSTRACT:

The present invention relates to the discovery of a novel erbB receptor ligand, referred to hereinafter as "cdGF", which protein has apparently broad involvement in the formation and maintenance of ordered spatial arrangements of differentiated tissues in vertebrates, and can be used to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.
11 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

22. Document ID: US 5912137 A
Entry 22 of 88
File: USPT
Jun 15, 1999

US-PAT-NO: 5912137
DOCUMENT-IDENTIFIER: US 5912137 A

TITLE: Assays for protein kinases using fluorescent

DATE-ISSUED: June 15, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY
Tsien; Roger Y. | La Jolla | CA | N/A | N/A
Cubitt; Andrew B. | San Diego | CA | N/A | N/A

US-CL-CURRENT: 435/15; 530/350, 530/352, 536/23.4

ABSTRACT:

This invention provides assays for protein kinase activity using fluorescent proteins engineered to include sequences that can be phosphorylated by protein kinases. The proteins exhibit different fluorescent properties in the non-phosphorylated and phosphorylated states.
24 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 14

23. Document ID: US 5910415 A
Entry 23 of 88
File: USPT
Jun 8, 1999

US-PAT-NO: 5910415
DOCUMENT-IDENTIFIER: US 5910415 A

TITLE: Controlled modification of eukaryotic genomes

DATE-ISSUED: June 8, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY
Hodges; Thomas K. | West Lafayette | IN | N/A | N/A
Lyznik; Leszek A. | Johnston | IA | N/A | N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/410, 536/23.1, 800/266, 800/267, 800/278

ABSTRACT:

A method of using a unique DNA construct for the creation of transgenic eukaryotic cells is described. The method allows a more precise and effective transformation procedure that targets the insertion of a DNA sequence into a predetermined DNA locus, while enabling the removal of any randomly inserted DNA sequences that occur as a by product of known transformation procedures.
12 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

24. Document ID: US 5888981 A
Entry 24 of 88
File: USPT
Mar 30, 1999

US-PAT-NO: 5888981
DOCUMENT-IDENTIFIER: US 5888981 A

TITLE: Methods for regulating gene expression

DATE-ISSUED: March 30, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY
Bujard; Hermann | Heidelberg | N/A | N/A | DEX
Gossen; Manfred | El Cerrito | CA | N/A | N/A
Salfeld; Jochen G. | North Grafton | MA | N/A | N/A

Voss; Jeffrey W.
West Boylston
MA
N/A
N/A

US-CL-CURRENT: 514/44; 424/93.21, 435/455, 435/463, 435/465

ABSTRACT:

A method for regulating expression of a tet operator-linked gene in a cell of a subject is disclosed. In one embodiment, the method involves introducing into the cell a nucleic acid molecule encoding a tetracycline-controllable transactivator (tTA), the tTA comprising a Tet repressor operably linked to a polypeptide which directly or indirectly activates transcription in eucaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject. Alternatively, in another embodiment, the method involves obtaining the cell from the subject, introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one tet operator sequence, introducing into the cell a second nucleic acid molecule encoding a tTA, to form a modified cell, administering the modified cell to the is subject, and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first and second nucleic acid molecule can be within a single molecule (e.g., in the same vector) or on separate molecules.
17 Claims, 36 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 32

25. Document ID: US 5888732 A
Entry 25 of 88
File: USPT
Mar 30, 1999

US-PAT-NO: 5888732
DOCUMENT-IDENTIFIER: US 5888732 A

TITLE: Recombinational cloning using engineered recombination sites

DATE-ISSUED: March 30, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY
Hartley; James L. | Frederick | MD | N/A | N/A
Brasch; Michael A. | Gaithersburg | MD | N/A | N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/91.42, 536/23.1, 536/24.2

ABSTRACT:

Recombinational cloning is provided by the use of nucleic acids, vectors and methods, in vitro and in vivo, for moving or exchanging segments of DNA molecules using engineered recombination sites and recombination proteins to provide chimeric DNA molecules that have the desired characteristic(s) and/or DNA segment(s).
47 Claims, 44 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 44

26. Document ID: US 5885776 A
Entry 26 of 88
File: USPT
Mar 23, 1999

US-PAT-NO: 5885776
DOCUMENT-IDENTIFIER: US 5885776 A

TITLE: Glaucoma compositions and therapeutic and diagnositic uses therefor

DATE-ISSUED: March 23, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY
Stone; Edwin M. | Iowa City | IA | N/A | N/A
Sheffield; Val C. | Coralville | IA | N/A | N/A
Alward; Wallace L. M. | Iowa City | IA | N/A | N/A

US-CL-CURRENT: 435/6

ABSTRACT:

Methods and compositions for treating glaucoma; and glaucoma diagnostics are disclosed.
37 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

27. Document ID: US 5882888 A
Entry 27 of 88
File: USPT
Mar 16, 1999

US-PAT-NO: 5882888
DOCUMENT-IDENTIFIER: US 5882888 A

TITLE: DNA integration by transposition

DATE-ISSUED: March 16, 1999

INVENTOR-INFORMATION:
NAME | CITY | STATE | ZIP CODE | COUNTRY

J.o slashed.rgensen; Steen Troels
Aller.o slashed.d
N/A
N/A
DKX

US-CL-CURRENT: 435/69.1; 435/243, 435/252.31, 435/320.1, 435/473, 435/477, 435/478, 435/489, 435/91.4, 536/23.1, 536/24.2

ABSTRACT:

Multicopy strains of gram-positive bacteria carrying multiple copies of a DNA sequence of interest may be constructed by use of a method involving introduction of a DNA construct comprising the DNA sequence of interest into the genome of the recipient cell by transposition and subsequent deletion of a marker gene used for selection of the cells having received the DNA construct by a resolution system. The multicopy strains are preferably free from a gene encoding an undesirable marker such as an antibiotic resistance marker.
6 Claims, 31 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 31

28. Document ID: US 5874283 A
Entry 28 of 88
File: USPT
Feb 23, 1999

US-PAT-NO: 5874283
DOCUMENT-IDENTIFIER: US 5874283 A

TITLE: Mammalian flap-specific endonuclease

DATE-ISSUED: February 23, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Harrington; John Joseph	Shaker Heights	OH	44120	N/A
Hsieh; Chih-Lin	St. Louis	MO	63131	N/A
Lieber; Michael R.	St. Louis	MO	63131	N/A

US-CL-CURRENT: 435/252.3; 435/199, 435/252.33, 435/320.1, 435/69.1, 530/350, 536/23.2 , 536/23.5

ABSTRACT:

Compositions comprising human FEN-1(flap) endonucleases, nucleic acids encoding them, and methods for their use are provided.
6 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

29. Document ID: US 5869239 A
Entry 29 of 88
File: USPT
Feb 9, 1999

US-PAT-NO: 5869239
DOCUMENT-IDENTIFIER: US 5869239 A

TITLE: Library screening method

DATE-ISSUED: February 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Treco; Douglas A.	Arlington	MA	N/A	N/A
Miller; Allan M.	Medford	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/477, 435/482, 435/490, 435/91.4, 435/91.41

ABSTRACT:

Materials and methods for homologous-recombination screening of DNA libraries constructed in a eukaryotic host and methods for homologous-recombination chromosome walking for isolating overlapping DNA sequences for building an extended physical map of a chromosomal region.
41 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

30. Document ID: US 5866755 A
Entry 30 of 88
File: USPT
Feb 2, 1999

US-PAT-NO: 5866755
DOCUMENT-IDENTIFIER: US 5866755 A

TITLE: Animals transgenic for a tetracycline-regulated transcriptional inhibitor

DATE-ISSUED: February 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A	

N/A

US-CL-CURRENT: 800/9; 800/18

ABSTRACT:

Transgenic animals carrying a transgene comprising a nucleic acid molecule encoding protein useful for regulating the expression of genes in eukaryotic cells and organisms in a highly controlled manner are disclosed. In the regulatory system of the invention, transcription of a tet operator-linked nucleotide sequence is inhibited by a transcriptional inhibitor fusion protein composed of two polypeptides, a first polypeptide which binds to tet operator sequences and a second polypeptide which directly or indirectly inhibits transcription in eukaryotic cells. In various embodiment, the first polypeptide binds to tet operator sequences either: (i) in the absence but not the presence of tetracycline (or an analogue thereof) or (ii) in the presence but not the absence of tetracycline (or an analogue thereof). In a preferred embodiment, the transgene encoding the transcriptional inhibitor fusion protein is integrated at a predetermined location within the chromosome of the transgenic animal.
25 Claims, 18 Drawing figures
Exemplary Claim Number: 1,2,3
Number of Drawing Sheets: 15

31. Document ID: US 5859310 A
Entry 31 of 88
File: USPT
Jan 12, 1999

US-PAT-NO: 5859310
DOCUMENT-IDENTIFIER: US 5859310 A

TITLE: Mice transgenic for a tetracycline-controlled transcriptional activator

DATE-ISSUED: January 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A	N/A
Salfeld; Jochen G.	Noth Graton	MA	N/A	N/A
Voss; Jeffrey W.	West Boylson	MA	N/A	N/A

US-CL-CURRENT: 800/9; 435/320.1, 435/325, 435/69.1, 435/70.1, 514/152, 536/23.4, 536/24.1, 800/18, 800/22, 800/25, 800/4

ABSTRACT:

Transgenic mice carrying two transgenes, the first coding for a transactivator fusion protein comprising a tet repressor and a polypeptide which directly or indirectly activates transcription of a tet operator-linked gene in eucaryotic cells, and the second comprising a gene operably linked to a minimal promotor operably linked to at least one tet operator sequence, are disclosed. Isolated DNA molecules (e.g., targeting vectors) for integrating a polynucleotide sequence encoding a transactivator of the invention at a predetermined location within a second target DNA molecule by homologous recombination are also disclosed. Transgenic mice having the DNA molecules of the invention integrated at a predetermined location in a chromosome by homologous recombination are also encompassed by the invention. Methods to regulate the expression of a tet operator linked-gene of interest by administering tetracycline or a tetracycline analogue to a mouse of the invention are also disclosed. The regulatory system of the invention allows for conditional inactivation or modulation of expression of a gene of interest in a host cell or mouse.
20 Claims, 36 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 32

32. Document ID: US 5840540 A
Entry 32 of 88
File: USPT
Nov 24, 1998

US-PAT-NO: 5840540
DOCUMENT-IDENTIFIER: US 5840540 A

TITLE: Nucleic acids encoding presenilin II

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
St. George-Hyslop; Peter H.	Toronto	N/A	N/A	CAX
Rommens; Johanna M.	Toronto	N/A	N/A	CAX
Fraser; Paul E.	Toronto	N/A	N/A	CAX

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 530/350, 536/23.1, 536/24.3

ABSTRACT:

The present invention describes the identification, isolation and cloning of two human presenilin

genes, PS-1 and PS-2, mutations in which lead to Familial Alzheimer's Disease. Also identified
are presenilin homologue genes in mice, C. elegans and D. melanogaster. Transcripts and products
of these genes are useful in detecting and diagnosing Alzheimer's disease, developing
therapeutics for treatment of Alzheimer's disease, as well as the isolation and manufacture of
the protein and the constructions of transgenic animals expressing the mutant genes.
31 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

33. Document ID: US 5830461 A
Entry 33 of 88
File: USPT
Nov 3, 1998

US-PAT-NO: 5830461
DOCUMENT-IDENTIFIER: US 5830461 A

TITLE: Methods for promoting wound healing and treating transplant-associated vasculopathy

DATE-ISSUED: November 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Billiar; Timothy R.	Pittsburgh	PA	N/A	N/A
Tzeng; Edith	Pittsburgh	PA	N/A	N/A
Shears, II; Larry L.	Bethel Park	PA	N/A	N/A
Geller; David A.	Pittsburgh	PA	N/A	N/A
Edington; Howard David James	Pittsburgh	PA	N/A	N/A

US-CL-CURRENT: 424/94.4; 424/94.1, 435/189

ABSTRACT:

The present invention provides a method of promoting the closure of a wound in a patient. This
method involves transferring exogenous iNOS to the region of the wound whereby a product of iNOS
is produced in the region of the wound to promote the closure of the wound.
8 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

34. Document ID: US 5844079 A
Entry 34 of 88
File: USPT
Dec 1, 1998

US-PAT-NO: 5844079
DOCUMENT-IDENTIFIER: US 5844079 A

TITLE: Vertebrate embryonic pattern-inducing proteins, and uses related thereto

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ingham; Philip W.	Summertown	N/A	N/A	GB2
McMahon; Andrew P.	Lexington	MA	N/A	N/A
Tabin; Clifford J.	Cambridge	MA	N/A	N/A

US-CL-CURRENT: 530/350; 435/252.3, 435/320.1, 435/69.1, 435/7.1, 530/300, 536/23.1, 536/23.5

ABSTRACT:

The present invention concerns the discovery that proteins encoded by a family of vertebrate
genes, termed here hedgehog-related genes, comprise morphogenic signals produced by embryonic
patterning centers, and are involved in the formation of ordered spatial arrangements of
differentiated tissues in vertebrates. The present invention makes available compositions and
methods that can be utilized, for example to generate and/or maintain an array of different
vertebrate tissue both in vitro and in vivo.
41 Claims, 22 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 21

35. Document ID: US 5849571 A
Entry 35 of 88
File: USPT
Dec 15, 1998

US-PAT-NO: 5849571
DOCUMENT-IDENTIFIER: US 5849571 A

TITLE: Latency active herpes virus promoters and their use

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Glorioso; Joseph C.				

Cheswick
PA
N/A
N/A
Fink; David J.
Pittsburgh
PA
N/A
N/A
Goins; William F.
Pittsburgh
PA
N/A
N/A

US-CL-CURRENT: 435/320.1; 435/456

ABSTRACT:

The application discloses the structure of a herpes virus promoter that by means of which one can
obtain the transcription of a non-herpes gene in a cell latently infected with a herpes virus. An
HSV-1 vector comprising a LAP2 promoter encoded by SEQ ID NO:1, or fragments of SEQ ID NO:1 which
have LAP 2 promoter activity regulating the expression of a heterologous gene is particularly
disclosed. The herpes virus is preferably used to obtain such expression in the neurons of the
peripheral nerves, and the ganglion cells of the cranial nerves. The invention teaches that
specific diseases and pathological conditions and the corresponding non-herpes genes wherein such
expression has practical value.
12 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

36. Document ID: US 5834202 A
Entry 36 of 88
File: USPT
Nov 10, 1998

US-PAT-NO: 5834202
DOCUMENT-IDENTIFIER: US 5834202 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: November 10, 1998

INVENTOR-INFORMATION:
NAME
CITY
STATE
ZIP CODE
COUNTRY
Auerbach; Jeffrey I.
Rockville
MD
N/A
N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/91.1, 435/91.2, 536/23.1, 536/24.2, 536/24.33

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the
amplification is performed under isothermal conditions. The invention also includes kits
containing reagents for conducting the method.
24 Claims, 19 Drawing figures

Exemplary Claim Number: 1
Number of Drawing Sheets: 19

37. Document ID: US 5849991 A
Entry 37 of 88
File: USPT
Dec 15, 1998

US-PAT-NO: 5849991
DOCUMENT-IDENTIFIER: US 5849991 A

TITLE: Mice homozygous for an inactivated .alpha. 1,3-galactosyl transferase gene

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:
NAME
CITY
STATE
ZIP CODE
COUNTRY
d'Apice; Anthony J. F.
Balwyn
N/A
N/A
AUX
Pearse; Martin J.
Mordialloc
N/A
N/A
AUX
Robins; Allan J.
Waterloo Corner
N/A
N/A
AUX
Crawford; Robert J.
West Lake Shores
N/A
N/A
AUX
Rathjen; Peter D.
Blackwood
N/A
N/A
AUX

US-CL-CURRENT: 800/8; 435/320.1, 435/354, 435/463, 800/17, 800/18, 800/21, 800/22, 800/24

ABSTRACT:

Human pre-formed xenoantibodies play an important role in the hyperacute rejection response in
human xenotransplantation. Disclosed are materials and methods for removing or neutralizing such
antibodies. Also disclosed are materials and methods for reducing or eliminating the epitopes in
the donor organs that are recognized by such antibodies. Such epitopes are formed as the result
of activity by the enzyme .alpha.-1,3 galactosyltransferase. The porcine gene encoding
.alpha.-1,3 galactosyltransferase is disclosed, as are materials and methods for inactivating
("knocking out") the .alpha.-1,3 galactosyltransferase gene in mammalian cells and embryos.
Included are nucleic acid constructs useful for inactivating the .alpha.-1,3
galactosyltransferase gene in a target cell. Also disclosed is a novel leukemia inhibitory factor
(T-LIF) that is useful for maintenance of embryonic stem cells and primordial germ cells in
culture.
13 Claims, 47 Drawing figures

Exemplary Claim Number: 5
Number of Drawing Sheets: 42

38. Document ID: US 5849989 A
Entry 38 of 88
File: USPT
Dec 15, 1998

US-PAT-NO: 5849989
DOCUMENT-IDENTIFIER: US 5849989 A

TITLE: Insulin promoter factor, and uses related thereto

DATE-ISSUED: December 15, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Edlund; Thomas	Ume.ang.	N/A	N/A	SEX

US-CL-CURRENT: 800/9; 800/18

ABSTRACT:

The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of novel a transcriptional regulatory factor, referred to hereinafter as "Insulin Promoter Factor 1" or "Ipf1".
13 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

39. Document ID: US 5814618 A
Entry 39 of 88
File: USPT
Sep 29, 1998

US-PAT-NO: 5814618
DOCUMENT-IDENTIFIER: US 5814618 A

TITLE: Methods for regulating gene expression

DATE-ISSUED: September 29, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A	N/A

US-CL-CURRENT: 514/44; 424/93.21

ABSTRACT:

Methods of regulating gene expression in subjects using tetracycline-responsive fusion proteins are disclosed. In one embodiment, the method involves introducing into a cell the subject a nucleic acid molecule encoding a fusion protein which inhibits transcription, the fusion protein comprising a first polypeptide which binds to a tet operator sequence, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first polypeptide can binds to a tet operator sequence in the absence, but not the presence, of tetracycline. Alternatively, the first polypeptide can binds to a tet operator sequence in the presence, but not the absence, of tetracycline. In another embodiment, the method of the invention involves obtaining a cell from a subject, introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one tet operator sequence, introducing into the cell a second nucleic acid molecule encoding an inhibitory fusion protein of the invention to form a modified cell, administering the modified cell to the subject and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first and second nucleic acid molecules can be linked or can be separate molecules.
30 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

40. Document ID: US 5807708 A
Entry 40 of 88
File: USPT
Sep 15, 1998

US-PAT-NO: 5807708
DOCUMENT-IDENTIFIER: US 5807708 A

TITLE: Conservin nucleic acid molecules and compositions

DATE-ISSUED: September 15, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Falb; Dean A.	Wellesley	MA	N/A	N/A
Gimeno; Carlos J.	Boston	MA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 536/23.1, 536/23.5

ABSTRACT:

The present invention relates to the discovery of novel conservin genes and polypeptides.
Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.
54 Claims, 4 Drawing figures

Exemplary Claim Number: 1
Number of Drawing Sheets: 4

41. Document ID: US 5800998 A
Entry 41 of 88
File: USPT
Sep 1, 1998

US-PAT-NO: 5800998
DOCUMENT-IDENTIFIER: US 5800998 A

TITLE: Assays for diagnosing type II diabetes in a subject

DATE-ISSUED: September 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Glucksmann; M. Alexandra	Somerville	MA	N/A	N/A

US-CL-CURRENT: 435/6; 514/44, 536/23.1, 536/23.5

ABSTRACT:

Assays for determining whether a subject has or is at risk for developing type II diabetes, which
are based on detecting the presence or absence of alterations in the hepatic nuclear factor 1
(HNF-1) gene or protein of the subject are disclosed.
6 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

42. Document ID: US 5801030 A
Entry 42 of 88
File: USPT
Sep 1, 1998

US-PAT-NO: 5801030
DOCUMENT-IDENTIFIER: US 5801030 A

TITLE: Methods and vectors for site-specific recombination

DATE-ISSUED: September 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
McVey; Duncan L.	Derwood	MD	N/A	N/A
Kovesdi; Imre	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/456; 435/320.1, 435/462, 536/23.1, 536/23.2

ABSTRACT:

The present invention provides methods for site-specific recombination in a cell, as well as
vectors which can be employed in such methods. The methods and vectors of the present invention
can be used to obtain persistent gene expression in a cell and to modulate gene expression.

One preferred method according to the invention comprises contacting a cell with a vector
comprising an origin of replication functional in mammalian cells located between first and
second recombining sites located in parallel. Another preferred method comprises, in part,
contacting a cell with a vector comprising first and second recombining sites in antiparallel
orientations such that the vector is internalized by the cell. In both methods, the cell is
further provided with a site-specific recombinase that effects recombination between the first
and second recombining sites of the vector.
47 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

43. Document ID: US 5795726 A
Entry 43 of 88
File: USPT
Aug 18, 1998

US-PAT-NO: 5795726
DOCUMENT-IDENTIFIER: US 5795726 A

TITLE: Methods for identifying compounds useful in treating type II diabetes

DATE-ISSUED: August 18, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Glucksmann; M. Alexandra	Somerville	MA	N/A	N/A

US-CL-CURRENT: 435/7.21; 435/4, 435/6, 435/8, 536/23.5

ABSTRACT:

Methods for identifying compounds, which modulate the bioactivity of human hepatic nuclear
factor-1 (HNF-1), and which are therefore useful in treating type II diabetes are disclosed.
10 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

44. Document ID: US 5795734 A
Entry 44 of 88
File: USPT
Aug 18, 1998

US-PAT-NO: 5795734
DOCUMENT-IDENTIFIER: US 5795734 A

TITLE: EPH receptor ligands, and uses related thereto

DATE-ISSUED: August 18, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Flanagan; John G.	Newton	MA	N/A	N/A
Cheng; Hwai-Jong	Boston	MA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 435/7.1, 530/300, 530/350, 536/23.1, 536/23.5

ABSTRACT:

The present invention relates to the discovery of a novel EPH receptor ligand, referred to hereinafter as "Elf-1", which protein has apparently broad involvement in the formation and maintenance of ordered spatial arrangements of differentiated tissues in vertebrates, and can be used to generate and/or maintain an array of different vertebrate tissue both in vitro and in vivo.

26 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 12

45. Document ID: US 5792833 A
Entry 45 of 88
File: USPT
Aug 11, 1998

US-PAT-NO: 5792833
DOCUMENT-IDENTIFIER: US 5792833 A

TITLE: E2 binding proteins

DATE-ISSUED: August 11, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Androphy; Elliot J.	Natick	MA	N/A	N/A
Breiding; David E.	Somerville	MA	N/A	N/A

US-CL-CURRENT: 530/350; 530/300

ABSTRACT:

E2-BP polypeptides, nucleic acids encoding E2-BP polypeptides, and uses thereof.

25 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

46. Document ID: US 5789156 A
Entry 46 of 88
File: USPT
Aug 4, 1998

US-PAT-NO: 5789156
DOCUMENT-IDENTIFIER: US 5789156 A

TITLE: Tetracycline-regulated transcriptional inhibitors

DATE-ISSUED: August 4, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	CA	N/A	N/A

US-CL-CURRENT: 435/6; 435/252.3, 435/320.1, 435/69.1, 435/69.7, 435/810, 536/23.4, 536/23.7, 536/24.1

ABSTRACT:

Nucleic acid molecules and proteins useful for regulating the expression of genes in eukaryotic cells and organisms in a highly controlled manner are disclosed. In the regulatory system of the invention, transcription of a tet operator-linked nucleotide sequence is inhibited by a transcriptional inhibitor fusion protein composed of two polypeptides, a first polypeptide which binds to tet operator sequences either (i) in the absence but not the presence of tetracycline (or an analogue thereof) or (ii) in the presence but not the absence of tetracycline (or an analogue thereof), and a second polypeptide which directly or indirectly inhibits transcription in eukaryotic cells. In one embodiment, the fusion protein comprises a Tet repressor operatively linked to a transcriptional silencer polypeptide. In another embodiment, the fusion protein comprises a mutated Tet repressor operatively linked to a transcriptional silencer polypeptide.

The fusion proteins of the invention are useful for reducing the level of transcription of a tet operator-linked target gene. Moreover, the fusion proteins of the invention can be used in combination with tetracycline-regulated transcriptional activator fusion proteins to allow for precise regulation of the expression of one or multiple target genes. Kits including the components of the regulatory system of the invention are also encompassed by the invention.

49 Claims, 14 Drawing figures
Exemplary Claim Number: 1,2,17,18,19
Number of Drawing Sheets: 12

47. Document ID: US 5780296 A
Entry 47 of 88
File: USPT
Jul 14, 1998

US-PAT-NO: 5780296
DOCUMENT-IDENTIFIER: US 5780296 A

TITLE: Compositions and methods to promote homologous recombination in eukaryotic cells and
organisms

DATE-ISSUED: July 14, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Holloman; William K.	Yorktown Heights	NY	N/A	N/A
Kmiec; Eric B.	Malvern	PA	N/A	N/A

US-CL-CURRENT: 435/320.1; 536/23.2

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to promote homologous
recombination in eukaryotic cells and expression vectors that can be used to transiently express
recombinases in target cells. One embodiment of the invention encompasses genetically engineered
nucleic acids that encode a non-naturally occurring recombinase that causes a greater rate of
recombination than does the naturally occurring recombinase. Recombinases from Ustilago maydis,
Saccharomyces cerevisiae are specifically included in the invention.
26 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

48. Document ID: US 5770384 A
Entry 48 of 88
File: USPT
Jun 23, 1998

US-PAT-NO: 5770384
DOCUMENT-IDENTIFIER: US 5770384 A

TITLE: Method for determining compound interaction with E2 binding proteins

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Androphy; Elliot J.	Natick	MA	N/A	N/A
Breiding; David E.	Somerville	MA	N/A	N/A

US-CL-CURRENT: 435/7.8; 435/5, 435/69.1, 435/69.7, 435/7.1, 435/7.93, 514/2, 530/300 , 530/350,
536/23.72

ABSTRACT:

E2-BP polypeptides, nucleic acids encoding E2-BP polypeptides, and uses thereof.
42 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

49. Document ID: US 5763240 A
Entry 49 of 88
File: USPT
Jun 9, 1998

US-PAT-NO: 5763240
DOCUMENT-IDENTIFIER: US 5763240 A

TITLE: In vivo homologous sequence targeting in eukaryotic cells

DATE-ISSUED: June 9, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Zarling; David A.	Menlo Park	CA	N/A	N/A
Sena; Elissa P.	Palo Alto	CA	N/A	N/A

US-CL-CURRENT: 435/463; 435/6, 435/91.1, 435/91.4

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous
complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a
eukaryotic cell by homologous pairing, particularly for altering an endogenous DNA sequence, such
as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain
embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a
linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active
eukaryotic cell, generating a DNA sequence-specific targeting of one or more chemical
substituents in an intact nucleus of a metabolically active eukaryotic cell, generally for
purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also
relates to compositions that contain exogenous targeting polynucleotides,

complementary pairs of
exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and
recombinase proteins used in the methods of the invention.
47 Claims, 16 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 8

50. Document ID: US 5756671 A
Entry 50 of 88
File: USPT
May 26, 1998

US-PAT-NO: 5756671
DOCUMENT-IDENTIFIER: US 5756671 A

TITLE: CDC37 cell-cycle regulatory protein, and uses related thereto

DATE-ISSUED: May 26, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gyuris; Jeno	Winchester	MA	N/A	N/A
Lamphere; Lou	Boston	MA	N/A	N/A
Draetta; Giulio	Milan	N/A	N/A	ITX

US-CL-CURRENT: 530/350; 530/300

ABSTRACT:

The present invention relates to the discovery in mammalian cells, particularly human cells, of a
novel CDK-binding protein, referred to herein as "cdc37". As described herein, this protein
functions to facilitate activation and accordingly functions in the modulation of cell-cycle
progression, and therefore ultimately of cell growth and differentiation. Moreover, binding data
indicated that cdc37 may function coordinately with other cell-cycle regulatory proteins, such as
of cyclin-dependent kinases (CDKs), src, p53 and erk kinases.
37 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

51. Document ID: US 5744336 A
Entry 51 of 88
File: USPT
Apr 28, 1998

US-PAT-NO: 5744336
DOCUMENT-IDENTIFIER: US 5744336 A

TITLE: DNA constructs for controlled transformation of eukaryotic cells

DATE-ISSUED: April 28, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hodges; Thomas K.	West Lafayette	IN	N/A	N/A
Lyznik; Leszek A.	West Lafayette	IN	N/A	N/A

US-CL-CURRENT: 435/320.1; 536/23.1, 536/24.1, 536/24.2

ABSTRACT:

DNA constructs are provided for the creation of transgenic eukaryotic cells. These DNA constructs
allow a more precise and effective transformation procedure by enabling the targeting of DNA
sequences for insertion into a particular DNA locus, while enabling the removal of any randomly
inserted DNA sequences that occur as a by product of known transformation procedures.
15 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

52. Document ID: US 5733733 A
Entry 52 of 88
File: USPT
Mar 31, 1998

US-PAT-NO: 5733733
DOCUMENT-IDENTIFIER: US 5733733 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: March 31, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Auerbach; Jeffrey I.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/320.1, 435/5, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.33

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the
amplification is performed under isothermal conditions. The invention also includes kits
containing reagents for conducting the method.
26 Claims, 19 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 19

53. Document ID: US 5721118 A
Entry 53 of 88
File: USPT
Feb 24, 1998

US-PAT-NO: 5721118
DOCUMENT-IDENTIFIER: US 5721118 A

TITLE: Mammalian artificial chromosomes and methods of using same

DATE-ISSUED: February 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Scheffler; Immo E.	Del Mar	CA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 435/449, 514/44, 536/23.1, 536/23.5

ABSTRACT:

The present invention provides a mammalian artificial chromosome (MAC), comprising a centromere and a unique cloning site, said MAC containing less than 0.1% of the DNA present in a normal haploid genome of the mammalian cell from which the centromere was obtained. The invention further provides a MAC, wherein the unique cloning site is a nucleic acid sequence encoding a selectable marker. The invention also provides methods of preparing a MAC. In addition, the invention provides methods of stably expressing a selectable marker in a cell, comprising introducing a MAC containing the selectable marker into the cell. The invention also provides a cell containing a MAC expressing an exogenous nucleic acid sequence and a transgenic mammal expressing a selectable marker.
17 Claims, 6 Drawing figures
Exemplary Claim Number: 2,7,17
Number of Drawing Sheets: 3

54. Document ID: US 5681559 A
Entry 54 of 88
File: USPT
Oct 28, 1997

US-PAT-NO: 5681559
DOCUMENT-IDENTIFIER: US 5681559 A

TITLE: Method for producing a highly enriched population of hematopoietic stem cells

DATE-ISSUED: October 28, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
DiGiusto; David	Palo Alto	CA	N/A	N/A
Galy; Anne	Palo Alto	CA	N/A	N/A

US-CL-CURRENT: 424/93.1; 424/93.7, 435/7.2, 435/7.21

ABSTRACT:

The present invention provides a simple and reliable means for isolating populations of hematopoietic cells enriched for stem cell activity on the basis of possession of high CD34 cell surface antigen density ("CD34hi"). CD34.sup.hi cell preparations are useful, for example, for drug discovery efforts, for reconstituting hematopoiesis in an animal lacking a functioning hematopoietic system, and for gene therapies.
17 Claims, 40 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

55. Document ID: US 5654168 A
Entry 55 of 88
File: USPT
Aug 5, 1997

US-PAT-NO: 5654168
DOCUMENT-IDENTIFIER: US 5654168 A

TITLE: Tetracycline-inducible transcriptional activator and tetracycline-regulated transcription units

DATE-ISSUED: August 5, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	Berkeley	CA	N/A	N/A

US-CL-CURRENT: 435/69.1; 435/320.1, 536/23.7, 536/24.1

ABSTRACT:

Nucleic acid molecules and proteins useful for regulating the expression of genes in eukaryotic cells and organisms in an inducible manner are disclosed. In the regulatory system of the invention, transcription of a tet operator-linked nucleotide sequence is stimulated by a transcriptional activator fusion protein composed of two polypeptides, a first polypeptide which binds to tet operator sequences in the presence of tetracycline or a tetracycline analogue and a second polypeptide which directly or indirectly activates transcription in eukaryotic cells. In one embodiment, the fusion protein comprises a mutated Tet repressor

operatively linked to a
transcriptional activation polypeptide, such as a portion of herpes simplex virus virion protein
16. In the absence of an inducing agent (tetracycline or a tetracycline analogue), transcription
of the tet operator-linked nucleotide sequence remains uninduced. In the presence of the inducing
agent, transcription of the tet operator-linked nucleotide sequence is stimulated by the
transactivator fusion protein of the invention. Novel transcription units which allow for
coordinate or independent tetracycline-regulated expression of two or more nucleotide sequences
by the transactivator fusion protein of the invention are also disclosed. Kits including the
components of the regulatory system of the invention are also encompassed by the invention.
33 Claims, 12 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 10

56. Document ID: US 5650298 A
Entry 56 of 88
File: USPT
Jul 22, 1997

US-PAT-NO: 5650298
DOCUMENT-IDENTIFIER: US 5650298 A

TITLE: Tight control of gene expression in eucaryotic cells by tetracycline-responsive promoters

DATE-ISSUED: July 22, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	Heidelberg	N/A	N/A	DEX
Salfeld; Jochen G.	North Grafton	MA	N/A	N/A
Voss; Jeffrey W.	Framingham	MA	N/A	N/A

US-CL-CURRENT: 435/69.7; 435/320.1, 435/463, 536/23.4, 536/24.1

ABSTRACT:

Transgenic animals carrying two transgenes, the first coding for a transactivator fusion protein
comprising a tet repressor and a polypeptide which directly or indirectly activates in eucaryotic
cells, and the second comprising a gene operably linked to a minimal promoter operably linked to
at least one tet operator sequence, are disclosed. Isolated DNA molecules (e.g., targeting
vectors) for integrating a polynucleotide sequence encoding a transactivator of the invention at
a predetermined location within a second target DNA molecule by homologous recombination are also
disclosed. Transgenic animals having the DNA molecules of the invention integrated at a
predetermined location in a chromosome by homologous recombination are also encompassed by the
invention. Methods to regulate the expression of a tet operator linked-gene of interest by
administering tetracycline or a tetracycline analogue to an animal of the invention are also
disclosed. The regulatory system of the invention allows for conditional inactivation or
modulation of expression of a gene of interest in a host cell or animal.
45 Claims, 36 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 32

57. Document ID: US 5635381 A
Entry 57 of 88
File: USPT
Jun 3, 1997

US-PAT-NO: 5635381
DOCUMENT-IDENTIFIER: US 5635381 A

TITLE: Agrobacterium bacteria capable of site-specific recombination

DATE-ISSUED: June 3, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hooykaas; Paul J. J.	Leiden	N/A	N/A	NLX
Mozo; Teresa	Berlin	N/A	N/A	DEX

US-CL-CURRENT: 800/294; 435/199, 435/252.2, 435/252.3, 435/320.1, 435/419, 435/477, 435/71.2,
536/23.72

ABSTRACT:

The invention provides Agrobacterium strains capable of producing a cite-specific recombinase
capable of effecting site-specific recombination of a first and a second recombination site in
Agrobacterium strains, when present therein, comprising a structural DNA sequence encoding said
recombinase and a DNA sequence capable of controlling expression in Agrobacterium strains. The
invention also provides methods for using the strains to transform plant cells.
20 Claims, 9 Drawing figures
Exemplary Claim Number: 1,16
Number of Drawing Sheets: 9

58. Document ID: US 5631237 A
Entry 58 of 88
File: USPT
May 20, 1997

US-PAT-NO: 5631237
DOCUMENT-IDENTIFIER: US 5631237 A

TITLE: Method for producing in vivo delivery of therapeutic agents via liposomes

DATE-ISSUED: May 20, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dzau; Victor J.	Los Altos Hills	CA	94022	N/A
Kaneda; Yasufumi	Suita-City, Osaka 565	N/A	N/A	JPX

US-CL-CURRENT: 514/44; 264/4.1, 264/4.3, 264/4.6, 424/417, 424/450, 428/402.2

ABSTRACT:

Methods and compositions are provided for intracellular transfer of a wide variety of agents, by using Sendai virus comprising liposomes having various compositions in the liposome lumen. A preferred method for preparing the liposomes provides for enhanced levels of luminal concentrations, as well as incorporation of high molecular weight molecules. The method comprises fusing liposomes, where one liposome comprises the Sendai virus proteins and the other liposome comprises the luminal composition. The subject methods find particular application with intranuclear transfer of nucleic acids, more particularly with cells of the vasculature.
10 Claims, 27 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 18

59. Document ID: US 5614389 A
Entry 59 of 88
File: USPT
Mar 25, 1997

US-PAT-NO: 5614389
DOCUMENT-IDENTIFIER: US 5614389 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: March 25, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Auerbach; Jeffrey I.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.
20 Claims, 19 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 19

60. Document ID: US 5612018 A
Entry 60 of 88
File: USPT
Mar 18, 1997

US-PAT-NO: 5612018
DOCUMENT-IDENTIFIER: US 5612018 A

TITLE: Drug screening and treatment for HIV thymocyte depletion

DATE-ISSUED: March 18, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bonyhadi; Mark L.	Belmont	CA	N/A	N/A
Kaneshima; Hideto	Palo Alto	CA	N/A	N/A
McCune; Joseph M.	San Francisco	CA	N/A	N/A
Namikawa; Reiko	Palo Alto	CA	N/A	N/A
Su; Lishan	Palo Alto	CA	N/A	N/A

US-CL-CURRENT: 424/9.2; 424/553, 424/577, 424/580, 424/582

ABSTRACT:

A method is provided for screening compounds for the ability to supress thymocyte depletion in thymuses of HIV-infected individuals, particularly enhancing the CD4.sup.+ -expressing population as compared to an untreated individual. Particularly, drugs are provided which allow for this result, cyclosporine A being exemplary.
7 Claims, 0 Drawing figures
Exemplary Claim Number: 1

61. Document ID: US 5591609 A
Entry 61 of 88

File: USPT

Jan 7, 1997

US-PAT-NO: 5591609
DOCUMENT-IDENTIFIER: US 5591609 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: January 7, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Auerbach; Jeffrey I.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1, 435/91.5

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.
15 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

62. Document ID: US 5589362 A
Entry 62 of 88

File: USPT

Dec 31, 1996

US-PAT-NO: 5589362
DOCUMENT-IDENTIFIER: US 5589362 A

TITLE: Tetracycline regulated transcriptional modulators with altered DNA binding specificities

DATE-ISSUED: December 31, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bujard; Hermann	Heidelberg	N/A	N/A	DEX
Gossen; Manfred	El Cerrito	N/A	N/A	DEX
Hillen; Wolfgang	Erlangen	N/A	N/A	DEX
Helbl; Vera	Fuerth	N/A	N/A	DEX
Schnappinger; Dirk	Bad Driburg	N/A	N/A	DEX

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 435/358, 435/455, 536/23.4, 536/24.1

ABSTRACT:

Isolated nucleic acid molecules encoding fusion proteins which regulate transcription in eukaryotic cells are disclosed. The fusion proteins of the invention comprise a Tet repressor having at least one amino acid mutation that confers on the fusion protein an ability to bind a class B tet operator sequence having a nucleotide substitution at position +4 or +6, operatively linked to a polypeptide which regulates transcription in eukaryotic cells. Methods for regulating transcription of a tet operator-linked gene in a cell are also provided. In one embodiment, the method involves introducing into the cell a nucleic acid molecule encoding a fusion protein which regulates transcription, the fusion protein comprising a Tet repressor having at least one amino acid mutation that confers on the fusion protein an ability to bind a class B tet operator sequence having a nucleotide substitution at position +4 or +6, operatively linked to a polypeptide which regulates transcription in eukaryotic cells, and modulating the concentration of a tetracycline, or analogue thereof, in contact with the cell.
20 Claims, 18 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

63. Document ID: US 5580734 A
Entry 63 of 88

File: USPT

Dec 3, 1996

US-PAT-NO: 5580734
DOCUMENT-IDENTIFIER: US 5580734 A

TITLE: Method of producing a physical map contigous DNA sequences

DATE-ISSUED: December 3, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Treco; Douglas A.	Arlington	MA	N/A	N/A
Miller; Allan M.	Medford	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/489

ABSTRACT:

Materials and methods for homologous-recombination screening of DNA libraries constructed in a

eukaryotic host and methods for homologous-recombination chromosome walking for isolating
overlapping DNA sequences for building an extended physical map of a chromosomal region.
4 Claims, 17 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

64. Document ID: US 5571688 A
Entry 64 of 88
File: USPT
Nov 5, 1996

US-PAT-NO: 5571688
DOCUMENT-IDENTIFIER: US 5571688 A

TITLE: Method of detecting gene expression

DATE-ISSUED: November 5, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mekalanos; John J.	Cambridge	MA	02138	N/A
Camilli; Andrew	Chestnut Hill	MA	02167	N/A

US-CL-CURRENT: 435/29; 435/34, 435/6

ABSTRACT:

A reporter system relating to in vivo expression technology was devised to aid in the
identification and study of genes that display temporal or spatial patterns of expression during
infection of host tissues. The method of this invention comprises constructing a strain or pool
of strains of a microorganism which contains an artificial cointegrate comprising a reporter gene
flanked by direct repeats of sequences to which a resolvase enzyme binds, thus catalyzing
excision of the reporter gene, and further contains a coding sequence under the control of a
promoter sequence which encodes transcripts, the expression of which are easily monitored in
vitro and which result in a permanent genetic change, excision of the reporter gene, that is
heritable and easily detectable subsequent to induction of the synthetic operon.
16 Claims, 17 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

65. Document ID: US 5527695 A
Entry 65 of 88
File: USPT
Jun 18, 1996

US-PAT-NO: 5527695
DOCUMENT-IDENTIFIER: US 5527695 A

TITLE: Controlled modification of eukaryotic genomes

DATE-ISSUED: June 18, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hodges; Thomas K.	West Lafayette	IN	N/A	N/A
Lyznik; Leszek A.	West Lafayette	IN	N/A	N/A

US-CL-CURRENT: 800/291; 435/320.1

ABSTRACT:

DNA constructs are provided for the creation of transgenic eukaryotic cells. These DNA constructs
allow a more precise and effective transformation procedure by enabling the targeting of DNA
sequences for insertion into a particular DNA locus, while enabling the removal of any randomly
inserted DNA sequences that occur as a by product of known transformation procedures.
6 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

66. Document ID: US 5512452 A
Entry 66 of 88
File: USPT
Apr 30, 1996

US-PAT-NO: 5512452
DOCUMENT-IDENTIFIER: US 5512452 A

TITLE: Selection of bacterial genes induced in host tissues

DATE-ISSUED: April 30, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mekalanos; John J.	Cambridge	MA	N/A	N/A
Camilli; Andrew	Chestnut Hill	MA	N/A	N/A

US-CL-CURRENT: 435/25; 435/6

ABSTRACT:

A reporter system relating to in vivo expression technology was devised to aid in the
identification and study of genes that display temporal or spatial patterns of

expression during
infection of host tissues. The method of this invention comprises integrating a site-specific DNA
recombinase expression vector, and a reporter gene that is permanently removable by the
recombinase, by way of homologous recombination into a microorganism's chromosome and inducing
the expression of a synthetic operon which encodes transcripts, the expression of which are
easily monitored in vitro and which result in a permanent genetic change, excision of the
reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic
operon.
16 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 11

67. Document ID: US 5434066 A
Entry 67 of 88
File: USPT
Jul 18, 1995

US-PAT-NO: 5434066
DOCUMENT-IDENTIFIER: US 5434066 A

TITLE: Modulation of CRE recombinase in the in vivo cloning of DNA

DATE-ISSUED: July 18, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bebee; Robert L.	Gaithersburg	MD	N/A	N/A
Hartley; James L.	Frederick	MD	N/A	N/A

US-CL-CURRENT: 435/475; 435/252.3, 435/252.33, 435/476

ABSTRACT:

Methods and recombinant vectors suitable for accomplishing the in vivo alteration of a nucleic
acid molecule are disclosed. The invention in particular discloses the use of recombinases such
as Cre to accomplish in vivo recombination.
7 Claims, 0 Drawing figures
Exemplary Claim Number: 1

68. Document ID: US 5354668 A
Entry 68 of 88
File: USPT
Oct 11, 1994

US-PAT-NO: 5354668
DOCUMENT-IDENTIFIER: US 5354668 A

TITLE: Methods for the isothermal amplification of nucleic acid molecules

DATE-ISSUED: October 11, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Auerbach; Jeffrey I.	Rockville	MD	20850	N/A

US-CL-CURRENT: 435/91.1; 435/6

ABSTRACT:

Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the
amplification is performed under isothermal conditions. The invention also includes kits
containing reagents for conducting the method.
22 Claims, 14 Drawing figures
Exemplary Claim Number: 20
Number of Drawing Sheets: 14

69. Document ID: US 5102797 A
Entry 69 of 88
File: USPT
Apr 7, 1992

US-PAT-NO: 5102797
DOCUMENT-IDENTIFIER: US 5102797 A

TITLE: Introduction of heterologous genes into bacteria using transposon flanked expression
cassette and a binary vector system

DATE-ISSUED: April 7, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tucker; William T.	Oakland	CA	N/A	N/A
Gutterson; Neal I.	Oakland	CA	N/A	N/A

US-CL-CURRENT: 435/473; 435/320.1

ABSTRACT:

This invention relates to a new method for inserting heterologous genes into the genome of a
bacteria using a combined plasmid. The combined plasmid provides a cis complementation of
transposase genes and transposable elements. The method involves the homologous recombination of
a carrier plasmid and a functions plasmid to form the combined plasmid. The carrier plasmid
contains a transposable element which flanks a generic expression cassette. The functions plasmid
comprises transposase genes which complement the transposable element on the carrier plasmid. The
combined plasmid is then transferred to a recipient and the recipient is

monitored for
integration of the generic expression cassette into the genome. The combined plasmid is
preferably created by an in vivo homologous recombination of the carrier and functions plasmids.
17 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

70. Document ID: US 4997757 A
Entry 70 of 88
File: USPT
Mar 5, 1991

US-PAT-NO: 4997757
DOCUMENT-IDENTIFIER: US 4997757 A

TITLE: Process for detecting potential carcinogens

DATE-ISSUED: March 5, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schiestl; Robert H.	Rochester	NY	N/A	N/A

US-CL-CURRENT: 435/6; 435/29

ABSTRACT:

There is provided a process for screening an agent in order to determine whether such agent
increases the frequency of genome rearrangement in living matter.

In the first step of this process, there is provided a viable species of Saccharomyces cerevisiae
yeast which comprises repeated genetic elements in its haploid genome. These repeated genetic
elements are selected from the group consisting of functional and non-functional genetic
elements; and these elements are sufficiently homologous so that, under ambient conditions, they
recombine with each other and give rise to an indentifiable genome rearrangement which is a
deletion.

In the second step of this process, the viable species of yeast is exposed to the agent to be
tested. Thereafter, it is plated onto a growth medium which, after the exposed yeast species
grows upon it, facilitates the identification of those yeast which have undergone said genome
rearrangement.

In the last step of the process, the extent to which the exposed species of yeast has undergone
genome rearrangement is determined.

Also disclosed is a the viable yeast strain used in said process, the plasmid used to construct
said strain, and a process for constructing said strain.
20 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

71. Document ID: US 4959317 A
Entry 71 of 88
File: USPT
Sep 25, 1990

US-PAT-NO: 4959317
DOCUMENT-IDENTIFIER: US 4959317 A

TITLE: Site-specific recombination of DNA in eukaryotic cells

DATE-ISSUED: September 25, 1990

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sauer; Brian L.	Greenville	DE	N/A	N/A

US-CL-CURRENT: 435/462; 435/254.2, 435/254.21, 435/320.1, 435/477, 435/69.1, 435/91.1 , 435/91.41

ABSTRACT:

A method for producing site-specific recombination of DNA in eukaryotic cells at regions
designated lox sites is disclosed.
40 Claims, 11 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

72. Document ID: JP 11225785 A
Entry 72 of 88
File: JPAB
Aug 24, 1999

PUB-NO: JP411225785A
DOCUMENT-IDENTIFIER: JP 11225785 A
TITLE: OPTIMIZATION OF CELL FOR ENDOGENOUS GENE ACTIVATION

PUBN-DATE: August 24, 1999

INVENTOR-INFORMATION:

NAME	COUNTRY
HONOLD, KONRAD	N/A
HOLTSCHKE, THOMAS	N/A
STERN, ANNE	N/A

INT-CL (IPC): C12 N 15/09; C12 N 5/10; C12 Q 1/68

ABSTRACT:

PROBLEM TO BE SOLVED: To optimize the expression of a nucleic acid in cells by transfecting cells
with a vector comprising a heteroexpression control sequence or the like, positive selection
marker gene, site-specific recombinase target sequence and sequence capable of homologous
recombination, followed by culturing the resultant cells.

SOLUTION: The expression of a nucleic acid sequence endogenous in eukaryocytes is optimized by

the following procedure: cells are transfected with a 1st vector comprising a 1st
heteroexpression control sequence and a sequence of a 1st amplification gene or the like,
positive selection marker gene, at least two target sequences of a site-specific recombinase,
adjacent to the above sequences, and such a DNA sequence as to be adjacent to the above sequences
and homologous with the nucleic acid portion in the genome of the cells so as to be capable of
homologous recombination; the resulting transfected cells are cultured under such conditions as
to cause the homologous recombination of the above vector, and the resulting cells are isolated.

COPYRIGHT: (C)1999,JPO

73. Document ID: JP 11225785 A
Entry 73 of 88
File: JPAB
Aug 24, 1999

PUB-NO: JP411225785A
DOCUMENT-IDENTIFIER: JP 11225785 A
TITLE: OPTIMIZATION OF CELL FOR ENDOGENOUS GENE ACTIVATION

PUBN-DATE: August 24, 1999

INVENTOR-INFORMATION:
NAME
COUNTRY
HONOLD, KONRAD
N/A
HOLTSCHKE, THOMAS
N/A
STERN, ANNE
N/A

INT-CL (IPC): C12 N 15/09; C12 N 5/10; C12 Q 1/68

ABSTRACT:

PROBLEM TO BE SOLVED: To optimize the expression of a nucleic acid in cells by transfecting cells
with a vector comprising a heteroexpression control sequence or the like, positive selection
marker gene, site-specific recombinase target sequence and sequence capable of homologous
recombination, followed by culturing the resultant cells.

SOLUTION: The expression of a nucleic acid sequence endogenous in eukaryocytes is optimized by
the following procedure: cells are transfected with a 1st vector comprising a 1st
heteroexpression control sequence and a sequence of a 1st amplification gene or the like,
positive selection marker gene, at least two target sequences of a site-specific recombinase,
adjacent to the above sequences, and such a DNA sequence as to be adjacent to the above sequences
and homologous with the nucleic acid portion in the genome of the cells so as to be capable of
homologous recombination; the resulting transfected cells are cultured under such conditions as
to cause the homologous recombination of the above vector, and the resulting cells are isolated.

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74. Document ID: US 5780296 A
Entry 74 of 88
File: EPAB
Jul 14, 1998

PUB-NO: US005780296A
DOCUMENT-IDENTIFIER: US 5780296 A
TITLE: Compositions and methods to promote homologous recombination in eukaryotic cells and
organisms
PUBN-DATE: July 14, 1998

INVENTOR-INFORMATION:
NAME
COUNTRY
HOLLOMAN, WILLIAM K
US
KMIEC, ERIC B
US

INT-CL (IPC): C12 N 15/63

EUR-CL (EPC): C12N009/00

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to promote homologous
recombination in eukaryotic cells and expression vectors that can be used to transiently express
recombinases in target cells. One embodiment of the invention encompasses genetically engineered
nucleic acids that encode a non-naturally occurring recombinase that causes a greater rate of
recombination than does the naturally occurring recombinase. Recombinases from Ustilago maydis,
Saccharomyces cerevisiae are specifically included in the invention.

75. Document ID: US 5763240 A
Entry 75 of 88
File: EPAB
Jun 9, 1998

PUB-NO: US005763240A
DOCUMENT-IDENTIFIER: US 5763240 A
TITLE: In vivo homologous sequence targeting in eukaryotic cells
PUBN-DATE: June 9, 1998

INVENTOR-INFORMATION:
NAME
COUNTRY
ZARLING, DAVID A
US
SENA, ELISSA P
US

INT-CL (IPC): C12 N 15/64; C12 N 15/90; C12 Q 1/68; C12 P 19/34

EUR-CL (EPC): C12N015/90

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous
complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a
eukaryotic cell by homologous pairing, particularly for altering an endogenous DNA sequence, such
as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain
embodiments, the invention relates to methods for targeting an exogenous

polynucleotide having a
linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active
eukaryotic cell, generating a DNA sequence-specific targeting of one or more chemical
substituents in an intact nucleus of a metabolically active eukaryotic cell, generally for
purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also
relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of
exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and
recombinase proteins used in the methods of the invention.

76. Document ID: WO 9811214 A1
Entry 76 of 88
File: EPAB
Mar 19, 1998

PUB-NO: WO009811214A1
DOCUMENT-IDENTIFIER: WO 9811214 A1
TITLE: MAMMALIAN AND HUMAN REC2
PUBN-DATE: March 19, 1998

INVENTOR-INFORMATION:
NAME
COUNTRY
HOLLOMAN, WILLIAM K
N/A
RICE, MICHAEL C
N/A
SMITH, SHERYL T
N/A
SHU, ZHIGANG
N/A
KMIEC, ERIC B
N/A

INT-CL (IPC): C12 N 15/12; C12 N 15/87; C12 P 19/34

EUR-CL (EPC): C12N009/00

ABSTRACT:

The invention concerns mammalian recombinase genes (REC2) and their promoters. Over expression of
REC2 in a cell is found to facilitate homologous recombination, particularly homologous
recombination using a DNA/RNA chimeric oligonucleotide and to sensitize a cell to the apoptotic
effects of irradiation. The REC2 promoter, in combination with a strong enhancer, e.g., a SV40
enhancer, was found to be a strong promoter following irridiation of the cells. A radiation
induceable promoter can be used to sensitize a cell to radiation treatment by operably linking
the radiation induceable promoter to a gene whose expression converts a prodrug to a drug such as
a herpes thymidine kinase gene.

77. Document ID: WO 9630498 A1
Entry 77 of 88
File: EPAB
Oct 3, 1996

PUB-NO: WO009630498A1
DOCUMENT-IDENTIFIER: WO 9630498 A1
TITLE: PRODUCTION OF ANTIBODIES USING CRE-MEDIATED SITE-SPECIFIC RECOMBINATION
PUBN-DATE: October 3, 1996

INVENTOR-INFORMATION:
NAME
COUNTRY
JAKOBOVITS, AYA
N/A
ZSEBO, KRISZTINA M
N/A

INT-CL (IPC): C12 N 5/00; C12 N 5/06; C12 N 5/16; C12 N 15/00; C12 N 15/06; C12 N 15/ 09; C12 N
15/13

EUR-CL (EPC): A01K067/027 ; C07K016/00 , C12N015/90

ABSTRACT:

A method to produce a cell expressing an antibody from a genomic sequence of a cell which has a
modified immunoglobulin locus is disclosed. The method takes advantage of Cre-mediated
site-specific recombination and homologous recombination. The method involves first introducing a
lox site into an immunoglobulin locus and then using the lox site as a target for introduction of
gene modifications via Cre-mediated in vivo recombination.

78. Document ID: WO 9622364 A1
Entry 78 of 88
File: EPAB
Jul 25, 1996

PUB-NO: WO009622364A1
DOCUMENT-IDENTIFIER: WO 9622364 A1
TITLE: COMPOSITIONS AND METHODS TO PROMOTE HOMOLOGOUS RECOMBINATION IN EUKARYOTIC CELLS AND ORGANISMS
PUBN-DATE: July 25, 1996

INVENTOR-INFORMATION:
NAME
COUNTRY
HOLLOMAN, WILLIAM K
N/A
KMIEC, ERIC B
N/A

INT-CL (IPC): C12 N 9/00; C12 N 9/22

EUR-CL (EPC): C12N009/00

ABSTRACT:

The invention concerns genes encoding recombinases that can be used to promote homologous
recombination in eukaryotic cells. The application teaches methods by which a recombinase of one
species can be used to isolate a homologous recombinase of a different species and methods to
identify the isolated homologs. Recombinases from Ustilago maydis and Saccharomyces cerevisiae
are specifically included in the invention. The invention encompasses the method of producing an
isolated recombinase protein in a prokaryotic cell and recovering the product in an active form.
The invention also encompasses a genetically engineered gene which encodes a non-naturally

occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. The invention further encompasses the use of recombinase proteins and of recombinase genes to promote homologous recombination, including recombination between a host cell genome and a chimeric oligonucleotide, i.e., an oligonucleotide having both RNA and DNA bases.

79. Document ID: US 5512452 A
Entry 79 of 88
File: EPAB
Apr 30, 1996

PUB-NO: US005512452A
DOCUMENT-IDENTIFIER: US 5512452 A
TITLE: Selection of bacterial genes induced in host tissues
PUBN-DATE: April 30, 1996

INVENTOR-INFORMATION:
NAME
COUNTRY
MEKALANOS, JOHN J
US
CAMILLI, ANDREW
US

INT-CL (IPC): C12 Q 1/02; C12 N 15/00

EUR-CL (EPC): C07K014/255 ; C12N015/10 , C12N015/52 , C12N015/62 , C12N015/90 , C12Q001/68

ABSTRACT:

A reporter system relating to in vivo expression technology was devised to aid in the identification and study of genes that display temporal or spatial patterns of expression during infection of host tissues. The method of this invention comprises integrating a site-specific DNA recombinase expression vector, and a reporter gene that is permanently removable by the recombinase, by way of homologous recombination into a microorganism's chromosome and inducing the expression of a synthetic operon which encodes transcripts, the expression of which are easily monitored in vitro and which result in a permanent genetic change, excision of the reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic operon.

80. Document ID: WO 9322443 A1
Entry 80 of 88
File: EPAB
Nov 11, 1993

PUB-NO: WO009322443A1
DOCUMENT-IDENTIFIER: WO 9322443 A1
TITLE: IN VIVO HOMOLOGOUS SEQUENCE TARGETING IN EUKARYOTIC CELLS
PUBN-DATE: November 11, 1993

INVENTOR-INFORMATION:
NAME
COUNTRY
ZARLING, DAVID A
N/A
SENA, ELISSA P
N/A

INT-CL (IPC): C12N 15/90; C12N 5/10; C12Q 1/68; G01N 33/68; A61K 48/00; A01K 67/027

EUR-CL (EPC): C12N015/90 ; C07K014/47 , C07K014/82

ABSTRACT:

The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a eukaryotic cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active eukaryotic cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active eukaryotic cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.

81. Document ID: WO 9937755 A2
Entry 81 of 88
File: DWPI
Jul 29, 1999

DERWENT-ACC-NO: 1999-458689
DERWENT-WEEK: 199938
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: New compositions and methods for targeting sequence modifications in related family genes
INVENTOR: LEHMAN, C W; PATI, S ; ZARLING, D ; ZENG, H

PRIORITY-DATA:
1997US-0070734
December 11, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9937755 A2	July 29, 1999	E	047	C12N015/00

INT-CL (IPC): C12 N 15/00

ABSTRACTED-PUB-NO: WO 9937755A
BASIC-ABSTRACT:

NOVELTY - A composition is new comprising at least one recombinase

and at least two
single-stranded targeting polynucleotides (I) which are substantially complementary to each other
and each having a consensus homology clamp for a gene family i.e. a homology motif tag (HMT).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method (A) for targeting a sequence modification in at least one member of a consensus
family of genes in a cell by homologous recombination. The method involves introducing into at
least one cell at least one recombinase and (I);

(2) a method (B) of making a non-human organism with a targeted sequence modification in at least
one member of a gene family by introducing into a cell at least one recombinase and (I). The
animal formed has at least one modification in at least one member of a consensus family of
genes;

(3) a method (C) of isolating a member of a gene family comprising a protein consensus sequence.
The method involves:

(a) adding the recombinase and (I) to a complex mixture of nucleic acids where the targeting
polynucleotides comprise a purification tag; and

(b) isolating the member using the purification tag; and

(4) a non-human organism containing a sequence modification in an endogenous consensus functional
domain of a gene member of a gene family.

USE - The composition is useful in kit form which include the composition as libraries or pools
of degenerate cssDNA probes along with other reagents such as recombinase etc. The methods and
compositions are used for inactivation of a gene family gene i.e. exogenous targeting
polynucleotides can be used to inactivate, decrease or alter the biological activity of one or
more genes in a cell (or transgenic nonhuman animal or plant). This is useful in the generation
of animal models of disease, or in the elucidation of gene function and activity. Alternatively,
the biological activity of the wild-type gene may be either decreased or the wild-type activity
altered to mimic disease states. This includes genetic manipulation of non-coding gene sequences
that affect the transcription of genes, including promoter, repressors, enhancers and
transcriptional activating sequences.

The compositions are useful in identifying new members of gene families which may be useful in
functional genomic studies as well as in identification of new drug targets. HMTs used in
homologous recombination methods can generate animals that have a wide variety of mutations in a
wide variety of related genes, potentially resulting in a wide variety of phenotypes including
those related to disease states. This may also be done on a cellular level to identify genes
involved in cellular phenotypes i.e. target identification.

ADVANTAGE - This invention provides compositions and methods for the evaluation and
characterization of individual and sets of genes in disease states.

Traditionally, exogenous sequences transferred into eukaryotic cells underwent homologous
recombination with homologous endogenous sequences only at very low frequencies. Hence they were
recombined inefficiently and large numbers of cells were needed to be transfected, selected and
screened in order to generate a correctly targeted homologous recombinant. Several proteins or
purified extracts having the property of promoting homologous recombination (recombinase
activity) have recently been identified and the frequency of homologous recombination is enhanced
by the presence of these recombinase activities. Such recent advances have resulted in techniques
allowing enhanced homologous recombination (EHR).

Relaxing the amount of sequence identity needed for homologous recombinati on allows greater
flexibility to target related genes for creating transgenic animals and cells containing
modifications in gene family consensus sequences.

82. Document ID: US 5948653 A, WO 9842727 A1, AU 9865620 A
Entry 82 of 88
File: DWPI
Sep 7, 1999

DERWENT-ACC-NO: 1998-542274
DERWENT-WEEK: 199943
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: Modification of target polynucleotide sequences - by homologous recombination using
recombinase and at least 2 single stranded polynucleot ides complementary to each other, used
for, e.g. correcting diseased alleles in cystic fibrosis
INVENTOR: PATI, S; ZARLING, D A

PRIORITY-DATA:
1997US-0910367
August 13, 1997
1997US-0041173
March 21, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5948653 A	September 7, 1999	N/A	000	C07H021/04
WO 9842727 A1	October 1, 1998	E	136	C07H021/04
AU 9865620 A	October 20, 1998	N/A	000	C07H021/04

INT-CL (IPC): C07 H 21/04; C07 K 14/00; C12 N 15/00; C12 P 19/34

ABSTRACTED-PUB-NO: US 5948653A
BASIC-ABSTRACT:

The following are claimed: (1) preparation of a targeted sequence modification (TSM) in a
preselected target DNA sequence in a eukaryotic zygote by homologous recombination, comprising
introducing into at least 1 eukaryotic zygote at least 1 recombinase and at least 2
single-stranded (ss) targeting polynucleotides (PNs) that are complementary

to each other, and
each having a homology clamp (HC) corresponding to or is complementary to a preselected target
DNA sequence; (2) preparation of TSM in a preselected target DNA sequence in a cell by homologous
recombination which contains an insertion, carried out as in (1), but where PNs also each have an
internal HC; (3) a method for targeting and altering, by homologous recombination, a pre-selected
target NA sequence in an extrachromosomal sequence (ExS) of a prokaryotic cell, comprising: (a)
adding to the extrachromosoma l sequence materials as in (1); (b) removing the recombinase, and
(c) introducing the altered element into a prokaryotic cell; (4) a method of generating a pool of
variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to ExS at
least 1 recombinase and pairs of ss targeting PNS which are complementary to each other and each
comprising HC corresponding to or being complementary to a preselected target NA sequence, the
pairs comprising a library of mismatches between the targeting PN and the target NA sequence, to
form a library of altered ExS's; (5) a method of generating a cellular library comprising variant
NA sequences of a pre-selected target NA sequence, comprising introducing into a population of
target cells materials as in (4), and (6) a method similar to (5) comprising: (a) adding to ExS
materials as in (4), to form altered ExS's; (b) as in (3b), and (c) introducing the altered
sequences into a population of a target cells to form the library of variant NA sequences.

USE - The method of (1) may be used for targeting and altering, by homologous recombination, a
pre-selected target nucleic acid (NA) sequence (claimed). The methods can provide for the
efficient and specific modification of targeted PNs. The methods can be used, e.g. to target
chemical substituents in a sequence-specific manner in vivo, to correct or to generate genetic
mutations in endogenous DNA sequences by homologous recombination and/or gene conversion, to
produce homologously targeted transgenic organisms, including animals and plants at high
efficiency, and in other application, e.g. targeted drug delivery, based on in vivo homologous
pairing. The methods can be used for correcting disease alleles involved in producing human
genetic diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g.
neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53) or
acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B virus
(HBV) infection.
ABSTRACTED-PUB-NO:

WO 9842727A EQUIVALENT-ABSTRACTS:

The following are claimed: (1) preparation of a targeted sequence modification (TSM) in a
preselected target DNA sequence in a eukaryotic zygote by homologous recombination, comprising
introducing into at least 1 eukaryotic zygote at least 1 recombinase and at least 2
single-stranded (ss) targeting polynucleotides (PNs) that are complementary to each other, and
each having a homology clamp (HC) corresponding to or is complementary to a preselected target
DNA sequence; (2) preparation of TSM in a preselected target DNA sequence in a cell by homologous
recombination which contains an insertion, carried out as in (1), but where PNs also each have an
internal HC; (3) a method for targeting and altering, by homologous recombination, a pre-selected
target NA sequence in an extrachromosomal sequence (ExS) of a prokaryotic cell, comprising: (a)
adding to the extrachromosoma l sequence materials as in (1); (b) removing the recombinase, and
(c) introducing the altered element into a prokaryotic cell; (4) a method of generating a pool of
variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to ExS at
least 1 recombinase and pairs of ss targeting PNS which are complementary to each other and each
comprising HC corresponding to or being complementary to a preselected target NA sequence, the
pairs comprising a library of mismatches between the targeting PN and the target NA sequence, to
form a library of altered ExS's; (5) a method of generating a cellular library comprising variant
NA sequences of a pre-selected target NA sequence, comprising introducing into a population of
target cells materials as in (4), and (6) a method similar to (5) comprising: (a) adding to ExS
materials as in (4), to form altered ExS's; (b) as in (3b), and (c) introducing the altered
sequences into a population of a target cells to form the library of variant NA sequences.

USE - The method of (1) may be used for targeting and altering, by homologous recombination, a
pre-selected target nucleic acid (NA) sequence (claimed). The methods can provide for the
efficient and specific modification of targeted PNs. The methods can be used, e.g. to target
chemical substituents in a sequence-specific manner in vivo, to correct or to generate genetic
mutations in endogenous DNA sequences by homologous recombination and/or gene conversion, to
produce homologously targeted transgenic organisms, including animals and plants at high
efficiency, and in other application, e.g. targeted drug delivery, based on in vivo homologous
pairing. The methods can be used for correcting disease alleles involved in producing human
genetic diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g.
neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53) or
acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B virus
(HBV) infection.

83. Document ID: CA 2216596 A, AU 9739226 A, EP 841402 A2, JP 10155485 A, AU 694393 B, AU 9868048 A
Entry 83 of 88
File: DWPI
Mar 26, 1998

DERWENT-ACC-NO: 1998-251707
DERWENT-WEEK: 199927
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: Shuttle vector for transforming plants with large DNA fragments - contains T-DNA border
sequences and Ri ori origin of replication
INVENTOR: KAWASAKI, S

PRIORITY-DATA:
1996JP-0255184
September 26, 1996

PATENT-FAMILY:
PUB-NO PUB-DATE LANGUAGE PAGES MAIN-IPC
CA 2216596 A

	March 26, 1998		
		N/A	
			000
			C12N015/84
AU 9739226 A			
	April 2, 1998		
		N/A	
			041
			C12N015/03
EP 841402 A2			
	May 13, 1998		
		E	
			000
			C12N015/82
JP 10155485 A			
	June 16, 1998		
		N/A	
			050
			C12N015/09
AU 694393 B			
	July 16, 1998		
		N/A	
			000
			C12N015/03
AU 9868048 A			
	July 30, 1998		
		N/A	
			000
			C12N015/03

INT-CL (IPC): A01 H 5/00; C07 K 14/415; C12 N 1/20; C12 N 1/21; C12 N 5/10; C12 N 15/ 01; C12 N 15/03; C12 N 15/09; C12 N 15/10; C12 N 15/63; C12 N 15/68; C12 N 15/82; C12 N 15/84; C12 Q 1/68; C12 N 15/09; C12 R 1/91; C12 N 5/ 10; C12 R 1/91

ABSTRACTED-PUB-NO: AU 9739226A

BASIC-ABSTRACT:

High-capacity binary shuttle vector comprising T-DNA region and only Ri ori, or Ri ori and RK2 ori as the replication origin is new. Also claimed are: (i) a binary vector comprising a lox site in T-DNA region, a par C gene and an Ri ori replication origin, where the vector is capable of integrating a clone plasmid of a circular genome library with lox site by cre enzyme in an E. coli or Agrobacterium host; (ii) a binary vector for plant transformation comprising a multi-cloning site sandwiched by with a promoter and a terminator for plants in a T-DNA region and an Ri ori as replication origin; (iii) a genomic library having the ability to transform plants, preferably monocotyledonous plants; (iv) a genomic library having the ability to transform plants, where the library comprises a high-capacity binary shuttle vector as above; (v) a complementation method for assessing the function of genes in a genome fragment inserted into a clone of the genomic library of (iv), comprising i introducing the vector into an Agrobacterium cell and transferring the Agrobacterium into a plant; (vi) a complementation method for assessing the function of genes in a genome fragment inserted into a clone of a genomic library comprising integrating a plasmid clone constituting a library and a binary vector as above, where the library is constructed using a circular vector having a lox site and has E. coli as a host, introducing the integrated vector into an Agrobacterium cell and transferring the cell into a plant; (vii) a gene obtained with the method of (v) and (vi); (viii) a method for screening a useful gene comprising using a high-capacity binary shuttle vector as above; (ix) a transformed plant made using a binary vector as above or by introduction of the genes obtained in (vii); (x) a method for producing a high-efficiency Agrobacterium with recA- to maintain stably the binary vector with large insert comprising generating high transformation efficiency strains by the site-directed mutation on recA gene of said strain to transform to a recA- strain, introducing a homologous recombination to the strains with recA+ genes, between the transformed recA- vector and recA+ gene in the cell, selecting the recombinant by making a replica of the plate on which the strains are spread and irradiating the plate to screen a clone which can not grow under UV irradiation; and (xi) a high transformation efficiency Agrobacterium strain with recA+-, where the strain can maintain stably the high capacity binary vector with large insert.

USE - The methods and products are used to introduce genomic fragments of 10 kb or more into plants, including agriculturally important monocotyledonous plants.

ADVANTAGE - The processes are an alternative to forced introduction methods such as use of gene guns for intact cells or electroporation or polyethylene glycol methods for protoplasts. The former requires expensive facilities to process a small number of samples at a time, and the latter suffers from the drawback that regeneration from protoplasts to normal cells is difficult.

84. Document ID: KR 98703366 A, WO 9630498 A1, AU 9655310 A, EP 817835 A1, JP 11503015 W, AU 707813 B

Entry 84 of 88

File: DWPI

Oct 15, 1998

DERWENT-ACC-NO: 1996-485448

DERWENT-WEEK: 199950

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TITLE: Production of antibodies from cells with modified immunoglobulin locus - generated by Cre-mediated site-specific recombination to provide increased recombination efficiency

INVENTOR: JAKOBOVITS, A; ZSEBO, K M

PRIORITY-DATA:

1995US-0412826				
	March 29, 1995			

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
KR 98703366 A	October 15, 1998	N/A	000	C12N005/00
WO 9630498 A1	October 3, 1996	E	060	C12N005/00
AU 9655310 A	October 16, 1996	N/A	000	C12N005/00
EP 817835 A1	January 14, 1998	E		

000
C12N005/00
JP 11503015 W
March 23, 1999
N/A
048
C12N015/09
AU 707813 B
July 22, 1999
N/A
000
C12N005/00

INT-CL (IPC): C12 N 5/00; C12 N 5/06; C12 N 5/10; C12 N 5/16; C12 N 15/00; C12 N 15/ 06; C12 N
15/09; C12 N 15/13; C12 P 21/02

ABSTRACTED-PUB-NO: WO 9630498A
BASIC-ABSTRACT:

A cell expressing an antibody (Ab) from a genomic sequence contg. a modified immunoglobulin (Ig)
locus, is produced using Cre-mediated site-specific recombination to modify the locus by: (a)
transfecting an Ab-producing cell with a first homology-targeting vector contg. a first lox site
and a targeting sequence homologous to a first DNA sequence adjacent to the region of the Ig
locus to be modified, so that the lox site is inserted into the genomic sequence via
site-specific homologous recombination with genomic DNA in vivo; (b) transfecting the cell with a
lox-targeting vector comprising a second lox site suitable for Cre-mediated recombination with
the first lox site, and a sequence to modify the Ig locus; (c) interacting the lox sites with Cre
so that the modifying sequence inserts into the genomic sequence via Cre-mediated site-specific
recombination of the lox sites, thus modifying the Ig locus; and (d) selecting a transfectant
with a modified Ig locus which produces the Ab.

USE - The method allows the prodn. of cells expressing modified Ab, e.g. having the constant or
variable region modified, for class-switching an Ab or to alter the antigen specificity of the
Ab.

ADVANTAGE - The method provides increased efficiency of recombination (Cre-mediated recombination
ranges from 2-3% recombination events) over previous methods of modifying Ig loci directly in
Ab-producing cells using only homologous recombination for modifying the loci (ca. 0.39-0.75%
recombination).

85. Document ID: US 5945339 A, WO 9622364 A1, AU 9646960 A, US 5780296 A, EP 873402 A1
Entry 85 of 88
File: DWPI
Aug 31, 1999

DERWENT-ACC-NO: 1996-354521
DERWENT-WEEK: 199942
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: Isolated recombinase enzyme and gene - obtd. from Ustilago maydis, used to promote
homologous recombination in eukaryotic cells
INVENTOR: HOLLOMAN, W K; KMIEC, E B

PRIORITY-DATA:
1995US-0373134
January 17, 1995
1998US-0114637
July 13, 1998

PATENT-FAMILY:
PUB-NO
PUB-DATE
LANGUAGE
PAGES
MAIN-IPC
US 5945339 A
August 31, 1999
N/A
000
C12N015/64
WO 9622364 A1
July 25, 1996
E
071
C12N009/00
AU 9646960 A
August 7, 1996
N/A
000
C12N009/00
US 5780296 A
July 14, 1998
N/A
000
C12N015/63
EP 873402 A1
October 28, 1998
E
000
C12N009/00

INT-CL (IPC): C12 N 9/00; C12 N 9/22; C12 N 15/63; C12 N 15/64

ABSTRACTED-PUB-NO: US 5780296A
BASIC-ABSTRACT:

Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater
than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of
polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d)
has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino
acid.

USE - The prods. and methods can be used to promote HR in cells for, e.g. making specific genetic
alterations in cells to produce a recombinant protein, introducing specific alterations in
embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in
vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in
culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a
human subject in need of gene therapy for a medical condition.
ABSTRACTED-PUB-NO:

US 5945339A EQUIVALENT-ABSTRACTS:

Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater
than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of
polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d)
has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino
acid.

USE - The prods. and methods can be used to promote HR in cells for, e.g.

making specific genetic
alterations in cells to produce a recombinant protein, introducing specific alterations in
embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in
vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in
culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a
human subject in need of gene therapy for a medical condition.

Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by SDS-PAGE of greater
than 70 kD; (b) catalyses the formation of complementary or identical strand pairings of
polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR) in a eukaryote; and (d)
has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino
acid.

USE - The prods. and methods can be used to promote HR in cells for, e.g. making specific genetic
alterations in cells to produce a recombinant protein, introducing specific alterations in
embryonic stem cells or ova to be used in the construction of transgenic animals, modifying in
vitro explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in
culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into a
human subject in need of gene therapy for a medical condition.

WO 9622364A

86. Document ID: US 5910415 A, WO 9417176 A1, EP 686191 A1, US 5527695 A, US 5744336 A
Entry 86 of 88
File: DWPI
Jun 8, 1999

DERWENT-ACC-NO: 1994-264090
DERWENT-WEEK: 199930
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: DNA constructs - for creating transgenic eukaryotic cells
INVENTOR: HODGES, T K; LYZNIK, L A

PRIORITY-DATA:
1993US-0010997
January 29, 1993
1996US-0612551
March 8, 1996
1998US-0006232
January 13, 1998

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5910415 A	June 8, 1999	N/A	000	C12Q001/68
WO 9417176 A1	August 4, 1994	E	079	C12N005/00
EP 686191 A1	December 13, 1995	E	000	C12N005/00
US 5527695 A	June 18, 1996	N/A	027	C12N015/00
US 5744336 A	April 28, 1998	N/A	028	C07H021/04

INT-CL (IPC): A01 H 1/04; A01 H 4/00; A01 H 5/00; A01 H 5/10; C07 H 21/04; C12 N 5/00 ; C12 N 15/00; C12 N 15/09; C12 N 15/63; C12 N 15/82; C12 Q 1/68

ABSTRACTED-PUB-NO: US 5527695A
BASIC-ABSTRACT:

The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a)
a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably
linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of
interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of
directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for
inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA
sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s
recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination
into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and
flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable
selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s
recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of
eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly
repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic
cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable
marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA
sequence targeted for inversion into the eukaryotic cell having less than or equal to 1
polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell
sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences.

Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in
vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly
selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's
DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to
isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA
constructs; (d) applying selection means to isolate cells having the targeted DNA sequence
integrated into the organism's DNA via a homologous recombination event; (e) removing the
excisable selection region; and (f) culturing the resultant cells to regenerate an entire
organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing

an inducible
promoter.

USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's
DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a
specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed)
contg. a DNA sequence of interest, utilising (I), (II) or (III).
ABSTRACTED-PUB-NO:

US 5744336A EQUIVALENT-ABSTRACTS:

A method for the production of fertile, transgenic plants wherein the transgenic plant has a DNA
sequence of interest integrated at a predetermined DNA sequence of the plant, said method
comprising the steps of

introducing into plant cells a DNA construct comprising

a multifunctional DNA sequence flanked by a pair of directly repeated site-specific recombination
sequences,

said multifunctional DNA sequence comprising a gene encoding a selectable marker, and a DNA
sequence of interest,

wherein said DNA sequence of interest is flanked by nucleotide sequences sharing homology to the
predetermined nucleotide sequence present in the plant cell, and the selectable marker gene is
operably linked to regulatory sequences capable of expressing the gene in the plant cell,

selecting for plant cells having said DNA construct integrated into the DNA of the plant cell,

eliminating randomly inserted DNA constructs through expression of a recombinase gene capable of
initiating recombination at the site-specific recombinase sequences in the plant cells,

identifying cells having said DNA sequence of interest integrated into the plant's DNA via a
homologous recombination event, and

culturing said identified cells to generate an entire plant.

The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a)
a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably
linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of
interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of
directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for
inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA
sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s
recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination
into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and
flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable
selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s
recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of
eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly
repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic
cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable
marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA
sequence targeted for inversion into the eukaryotic cell having less than or equal to 1
polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell
sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences.

Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in
vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly
selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's
DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to
isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA
constructs; (d) applying selection means to isolate cells having the targeted DNA sequence
integrated into the organism's DNA via a homologous recombination event; (e) removing the
excisable selection region; and (f) culturing the resultant cells to regenerate an entire
organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible
promoter.

USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's
DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a
specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed)
contg. a DNA sequence of interest, utilising (I), (II) or (III).

US 5910415A

The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a)
a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably
linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of
interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of
directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for
inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA
sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s
recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination
into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and
flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable
selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s
recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of
eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly
repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic
cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable
marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA
sequence targeted for inversion into the eukaryotic cell having less than or equal to 1
polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell

sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences.

Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter.

USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III).

WO 9417176A

87. Document ID: US 5763240 A, WO 9322443 A1, AU 9341156 A, JP 07506252 W, EP 672159 A1
Entry 87 of 88
File: DWPI
Jun 9, 1998

DERWENT-ACC-NO: 1993-368802
DERWENT-WEEK: 199830
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: In vivo homologous sequence targeting in eukaryotic cells - using a targeting polynucleotide and recombinase to deliver agents or alter genes
INVENTOR: SENA, E P; ZARLING, D A

PRIORITY-DATA:
1992US-0939767 September 2, 1992
1992US-0873438 April 24, 1992
1994US-0275916 July 14, 1994

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5763240 A	June 9, 1998	N/A	000	C12N015/64
WO 9322443 A1	November 11, 1993	E	100	C12N015/90
AU 9341156 A	November 29, 1993	N/A	000	C12N015/90
JP 07506252 W	July 13, 1995	N/A	027	C12N015/09
EP 672159 A1	September 20, 1995	E	000	C12N015/90

INT-CL (IPC): A01 K 67/027; A61 K 48/00; C12 N 5/10; C12 N 15/09; C12 N 15/64; C12 N 15/90; C12 P 19/34; C12 Q 1/68; G01 N 33/68

ABSTRACTED-PUB-NO: US 5763240A
BASIC-ABSTRACT:

A method is claimed for targeting and altering, by homologous recombinatio n, a pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence modification, comprising (a) introducing into at least one eukaryotic cell at least one recombinase and at least one targeting polynucleotide having a homology clamp that corresponds to or is complementary to a preselected target DNA sequence and (b) identifying a eukaryotic cell having a targeted DNA sequence modification at a preselected target DNA sequence. Also claimed are (A) a compsn. for producing a targeted modification of an endogenous DNA sequence, comprising a targeting polynucleotide and a recombinase; (B) a compsn. for producing a targeted sequence modification of a human disease allele; a targeting polynucleotide contg. a corrected sequence a recombinase or an expression polynucleotide that encodes and expresses a recombinase; (C) a kit for therapy, monitoring or prophylaxis of a genetic disease comprising a recombinase and a targeting polynucleotide; (D) a method for treating a disease of an animal harbouring a disease allele, comprising administering a compsn. consisting of: (a) a recombinase or an expression polynucleotide encoding a recombinase and (b) a targeting polynucleotide which produces a sequence modification upon homologous recombination with the disease allele; (E) an animal comprising an allele that has a sequence modification as in (D).

USE/ADVANTAGE - The method can be used to target chemical substits. (e.g. drugs) in a sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA sequence by homologous recombination and/or gene conversion or to produce homologously targeted transgenic animals at high efficiency. In partic., the method can be used for correcting disease alleles involved in human genetic diseases such as inherited genetic disease (e.g. cystic fibrosis) and neoplasm for treating or preventing viral diseases, by HBV hepatitis.
ABSTRACTED-PUB-NO:

WO 9322443A EQUIVALENT-ABSTRACTS:

A method is claimed for targeting and altering, by homologous recombinatio n, a pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence modification, comprising (a) introducing into at least one eukaryotic cell at least one recombinase and at least one targeting polynucleotide having a homology clamp that corresponds to or is complementary to a preselected

target DNA sequence and (b) identifying a eukaryotic cell having a targeted DNA sequence
modification at a preselected target DNA sequence. Also claimed are (A) a compsn. for producing a
targeted modification of an endogenous DNA sequence, comprising a targeting polynucleotide and a
recombinase; (B) a compsn. for producing a targeted sequence modification of a human disease
allele; a targeting polynucleotide contg. a corrected sequence a recombinase or an expression
polynucleotide that encodes and expresses a recombinase; (C) a kit for therapy, monitoring or
prophylaxis of a genetic disease comprising a recombinase and a targeting polynucleotide; (D) a
method for treating a disease of an animal harbouring a disease allele, comprising administering
a compsn. consisting of: (a) a recombinase or an expression polynucleotide encoding a recombinase
and (b) a targeting polynucleotide which produces a sequence modification upon homologous
recombination with the disease allele; (E) an animal comprising an allele that has a sequence
modification as in (D).

USE/ADVANTAGE - The method can be used to target chemical substits. (e.g. drugs) in a
sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous DNA
sequence by homologous recombination and/or gene conversion or to produce homologously targeted
transgenic animals at high efficiency. In partic., the method can be used for correcting disease
alleles involved in human genetic diseases such as inherited genetic disease (e.g. cystic
fibrosis) and neoplasm for treating or preventing viral diseases, by HBV hepatitis.

88. Document ID: EP 542466 A2, AU 655512 B, AU 9228316 A, CA 2082577 A, EP 542466 A3, JP 05336977 A, NZ 245070
A, ZA 9208662 A
Entry 88 of 88
File: DWPI
May 19, 1993

DERWENT-ACC-NO: 1993-160938
DERWENT-WEEK: 199320
COPYRIGHT 1999 DERWENT INFORMATION LTD
TITLE: Baculovirus transfer vector contg. locus of crossover PI sequence - as substrate for
recombinase enzyme, provides efficient homologous recombination with recombinant virus, esp. for
expression of polypeptide(s) for vaccines
INVENTOR: GEWERT, D R; PEAKMAN, T C

PRIORITY-DATA:
1991GB-0023929
November 11, 1991

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 542466 A2	May 19, 1993	E	018	C12N015/86
AU 655512 B	December 22, 1994	N/A	000	C12N015/86
AU 9228316 A	May 13, 1993	N/A	000	C12N015/86
CA 2082577 A	May 12, 1993	N/A	000	C12N015/86
EP 542466 A3	October 6, 1993	N/A	000	C12N015/86
JP 05336977 A	December 21, 1993	N/A	015	C12N015/86
NZ 245070 A	November 25, 1994	N/A	000	C12N015/74
ZA 9208662 A	July 27, 1994	N/A	036	C12N000/00

INT-CL (IPC): A61K 39/00; A61K 39/12; C12N 0/00; C12N 5/10; C12N 7/01; C12N 15/64; C12N 15/74;
C12N 15/86; G01N 33/53

ABSTRACTED-PUB-NO: EP 542466A
BASIC-ABSTRACT:

New baculovirus transfer vector contains a restriction site for insertion of a DNA sequence (I)
encoding a heterologous polypeptide (II); regulatory elements for expression of (I) when inserted
and a loXP (locus of crossolver PI) DNA sequence (III) to act as substrate for the Cre (causes
recombination) recombinase protein (N).

Also new are (1) recombinant DNA (V) comprising this vector and (I); (2) a baculovirus contg.
(III) as substrate for (IV); (3) recombinant baculovirus prepd. by homologous recombination of
the virus (2) and (V); (4) insect cells transfected with the recombinant virus; (5) vaccines
contg. (II) prepd. by culturing the transfected insect cells; and (6) test kits for detecting
(II)-specific antibodies or (II) themselves.

(III) is esp. of formula

5'-CCTTAATATAACTTCGTATAP
TGTATGCTATACGAAGTTATTAGGTCG 3'-GGAATTATATTGA
AGCATATTACA
TACGATATGCTTCAATAATCCAGC

USE/ADVANTAGE - The transfected cells provide high level expression of (II) which are useful in
human or veterinary medicine; in vaccines and in diagnostic assays. The transfer vector provides
an efficient in vitro system for constructing recombinant viruses which can be identified and
isolated. Up to 50 million recombinants can be produced from 1 microg plasmid DNA and up to 50%
of viral progeny are recombinants. If required inserted genes are easily recovered and
reinserted, and recombination efficiency is independent of gene size (which can be 10kb or
larger).

Term

Documents

1 SAME 2

88

including document number

Display Format:

09/203,500
Att #11

1. Document ID: US 6087107 A

L3: Entry 1 of 58

File: USPT

Jul 11, 2000

US-PAT-NO: 6087107
DOCUMENT-IDENTIFIER: US 6087107 A
TITLE: Therapeutics and diagnostics for congenital heart disease based on a novel human
transcription factor
DATE-ISSUED: July 11, 2000

US-CL-CURRENT: 435/6; 435/7.1, 536/24.31, 536/24.33

APPL-NO: 9/ 083351
DATE FILED: May 22, 1998

PARENT-CASE:
This application claims priority to provisional patent application 60/081,870, filed Apr. 15, 1998.

IN: Sheffield; Val C., Alward; Wallace L. M., Stone; Edwin M., Nishimura; Darryl, Patil; Shiva

AB: Methods and compositions for treating a congenital heart disease and methods and compositions for prognosing or diagnosing a congenital heart disease in a subject are disclosed.

2. Document ID: US 6074853 A

L3: Entry 2 of 58

File: USPT

Jun 13, 2000

US-PAT-NO: 6074853
DOCUMENT-IDENTIFIER: US 6074853 A
TITLE: Sequence alterations using homologous recombination
DATE-ISSUED: June 13, 2000

US-CL-CURRENT: 435/91.1; 435/455, 435/471

APPL-NO: 9/ 133934
DATE FILED: August 14, 1998

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This is a continuing application of U.S. application Ser. No. 08/910,367, filed Aug. 13, 1997 now U.S. Pat. No. 5,948,653, and claims the benefit of U.S. Provisional Application No. 60/041,173, filed Mar. 21, 1997.

IN: Pati; Sushma, Zarling; David A.

AB: The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a target cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active target cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active target cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.

3. Document ID: US 6066778 A

L3: Entry 3 of 58

File: USPT

May 23, 2000

US-PAT-NO: 6066778
DOCUMENT-IDENTIFIER: US 6066778 A
TITLE: Transgenic mice expressing APC resistant factor V
DATE-ISSUED: May 23, 2000

US-CL-CURRENT: 424/9.2

APPL-NO: 8/ 746111
DATE FILED: November 6, 1996

IN: Ginsburg; David, Cui; Jisong

AB: The present invention relates to compositions and methods for the screening of compounds for anticoagulant activity. In particular, the present invention relates to non-human transgenic animals expressing activated protein C ("APC")-resistant factor V proteins which display a predisposition toward spontaneous thrombosis. The present invention also provides methods for using these transgenic animals to screen compounds for anticoagulant activity.

4. Document ID: US 6046308 A

L3: Entry 4 of 58

File: USPT

Apr 4, 2000

US-PAT-NO: 6046308
DOCUMENT-IDENTIFIER: US 6046308 A
TITLE: Isolated TRBP polypeptides and uses therefor
DATE-ISSUED: April 4, 2000

US-CL-CURRENT: 530/350

APPL-NO: 9/ 360220

DATE FILED: July 23, 1999

PARENT-CASE:
RELATED APPLICATIONS This application is a divisional of U.S. patent application Ser. No.
08/840,164, which was filed on Apr. 11, 1997.

IN: Glucksmann; M. Alexandra

AB: The invention provides nucleic acids encoding a TRBP polypeptide, fragments
thereof and homologs thereof The invention also provides TRBP polypeptides, fragments
thereof and homologs thereof, and TRBP binding proteins. Methods for treating diseases or
conditions characterized by an aberrant TRBP activity, e.g., by administering to the subject
a TRBP therapeutic, are also disclosed. Diseases or conditions that can be treated according
to the methods of the invention include thyroid-related disorders, metabolic disorders, and
diabetes. Also disclosed are methods for predicting whether a subject is at risk of
developing a disease associated with an aberrant TRBP activity, by determining, e.g.,
whether the subject has a genetic lesion in a TRBP gene and assays for identifying TRBP
therapeutics.

5. Document ID: US 6037173 A

L3: Entry 5 of 58 File: USPT Mar 14, 2000

US-PAT-NO: 6037173
DOCUMENT-IDENTIFIER: US 6037173 A
TITLE: Isolated nucleic acid encoding TRBP
DATE-ISSUED: March 14, 2000

US-CL-CURRENT: 435/325; 435/320.1, 435/366, 536/23.1, 536/23.5, 536/24.31

APPL-NO: 8/ 840146
DATE FILED: April 11, 1997

IN: Glucksmann; M. Alexandra

AB: The invention provides nucleic acids encoding a TRBP polypeptide, fragments
thereof and homologs thereof The invention also provides TRBP polypeptides, fragments
thereof and homologs thereof, and TRBP binding proteins. Methods for treating diseases or
conditions characterized by an aberrant TRBP activity, e.g., by administering to the subject
a TRBP therapeutic, are also disclosed. Diseases or conditions that can be treated according
to the methods of the invention include thyroid-related disorders, metabolic disorders, and
diabetes. Also disclosed are methods for predicting whether a subject is at risk of
developing a disease associated with an aberrant TRBP activity, by determining, e.g.,
whether the subject has a genetic lesion in a TRBP gene and assays for identifying TRBP
therapeutics.

6. Document ID: US 6031076 A

L3: Entry 6 of 58 File: USPT Feb 29, 2000

US-PAT-NO: 6031076
DOCUMENT-IDENTIFIER: US 6031076 A
TITLE: Conservin compositions
DATE-ISSUED: February 29, 2000

US-CL-CURRENT: 530/350; 530/402, 536/23.1, 536/23.4, 536/23.5

APPL-NO: 9/ 002832
DATE FILED: January 5, 1998

PARENT-CASE:
RELATED APPLICATIONS This application is a divisional application of U.S. Ser. No. 08/688,609,
filed on Jul. 30, 1996, now U.S. Pat. No. 5,807,708 of all of the aforementioned application(s)
are hereby incorporated by reference.

IN: Falb; Dean A., Gimeno; Carlos J.

AB: The present invention relates to the discovery of novel conservin genes and
polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are
also disclosed.

7. Document ID: US 6015692 A

L3: Entry 7 of 58 File: USPT Jan 18, 2000

US-PAT-NO: 6015692
DOCUMENT-IDENTIFIER: US 6015692 A
TITLE: CDC37 cell-cycle regulatory protein and uses related thereto
DATE-ISSUED: January 18, 2000

US-CL-CURRENT: 435/69.1; 435/183, 435/252.3, 435/320.1, 435/325, 536/23.2

APPL-NO: 8/ 853733
DATE FILED: May 9, 1997

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation of U.S. Ser. No. 08/625,209 filed Apr. 1,
1996, now U.S. Pat. No. 5,756,671, which is a continuation-in-part of U.S. Ser. No. 08/466,679
filed Jun. 6, 1995, entitled "Cdc37 Cell-Cycle Regulatory Protein and Uses Related Thereto", now
abandoned, which is a continuation-in-part of U.S. Ser. No. 08/253,155 filed Jun. 2, 1994,
entitled "CDK4 Binding Proteins" now U.S. Pat. No. 5,691,147. The teachings of both U.S. Ser.
Nos. 08/253,155 and 08/466,679 are incorporated herein by reference.

IN: Gyuris; Jeno, Lamphere; Lou, Draetta; Giulio

AB: The present invention relates to the discovery in mammalian cells, particularly
human cells, of a novel CDK-binding protein, referred to herein as "cdc37". As described
herein, this protein functions to facilitate activation and accordingly finctions in the
modulation of cell-cycle progression, and therefore ultimately of cell growth and
differentiation. Moreover, binding data indicated that cdc37 may function coordinately with
other cell-cycle regulatory proteins, such as of cyclin-dependent kinases (CDKs), src, p53
and erk kinases.

8. Document ID: US 6008014 A

L3: Entry 8 of 58

File: USPT

Dec 28, 1999

US-PAT-NO: 6008014
DOCUMENT-IDENTIFIER: US 6008014 A
TITLE: Method of making lipid metabolic pathway compositions
DATE-ISSUED: December 28, 1999

US-CL-CURRENT: 435/69.1; 435/325, 435/455, 435/91.1, 536/23.1

APPL-NO: 8/ 707399
DATE FILED: September 4, 1996

IN: Gimeno; Carlos J., Acton; Susan

AB: The present invention relates to the discovery of novel genes encoding Lipid
Metabolic Pathway (LMP) polypeptides. Therapeutics, diagnostics and screening assays based
on these molecules are also disclosed.

9. Document ID: US 6001619 A

L3: Entry 9 of 58

File: USPT

Dec 14, 1999

US-PAT-NO: 6001619
DOCUMENT-IDENTIFIER: US 6001619 A
TITLE: Ubiquitin ligases, and uses related thereto
DATE-ISSUED: December 14, 1999

US-CL-CURRENT: 435/193; 536/23.2

APPL-NO: 8/ 539205
DATE FILED: October 4, 1995

IN: Beach; David, Caligiuri; Maureen G., Nefsky; Bradley

AB: The present invention relates to the discovery in eukaryotic cells of a ubiquitin
ligases. These proteins are referred to herein collectively as "pub" proteins for Protein
UBiquitin ligase, and individually as h-pub1, h-pub2 and s-pub1 for the human pub1 and pub2
and Schizosaccharomyces pombe pub1 clones, respectively. Pub1 proteins apparently play a
role in the ubiquitination of the mitotic activating tyrosine phosphatase cdc25, and thus
they may regulate the progression of proliferation in eukaryotic cells by activating the
cyclin dependent kinase complexes. In S. pombe, disruption of s-pub1 elevates the level of
cdc25 protein in vivo increasing the activity of the tyrosine kinases, wee1 and mik1,
required to arrest the cell-cycle. Loss of wee1 function in an S. pombe cell carrying a
disruption in the s-pub1 gene results in a lethal premature entry into mitosis; such lethal
phenotype can be rescued by the loss of cdc25 function. An ubiquitin thioester adduct of
s-pub1 can be isolated from S. pombe and disruption of s-pub1 dramatically reduces
ubiquitination of cdc25.

10. Document ID: US 5994070 A

L3: Entry 10 of 58

File: USPT

Nov 30, 1999

US-PAT-NO: 5994070
DOCUMENT-IDENTIFIER: US 5994070 A
TITLE: Trio molecules and uses related thereto
DATE-ISSUED: November 30, 1999

US-CL-CURRENT: 435/6; 435/320.1, 435/325, 435/69.1, 536/23.5, 536/24.31

APPL-NO: 8/ 826267
DATE FILED: March 27, 1997

PARENT-CASE:
This application claims the benefit of U.S. Provisional Application No. 60/014,214 filed Mar. 27,
1996.

IN: Streuli; Michel, Debant; Anne, Serra-Pages; Carles

AB: Nucleic acids encoding TRIO proteins, the TRIO proteins themselves, and active
portions thereof as described. In addition, antibodies immunoreactive with TRIO proteins,
and preparations of such compositions are provided. Diagnostic and therapeutic assays and
reagents for detecting and treating disorders involving, for example, aberrant expression
(or loss thereof) of the TRIO protein are described. Assays are provided for identifying
agents that modulate the biological function of TRIO proteins.

11. Document ID: US 5989804 A

L3: Entry 11 of 58

File: USPT

Nov 23, 1999

US-PAT-NO: 5989804
DOCUMENT-IDENTIFIER: US 5989804 A
TITLE: E6 binding proteins
DATE-ISSUED: November 23, 1999

US-CL-CURRENT: 435/5; 435/7.23, 435/7.6, 435/7.7, 435/7.71, 435/7.72, 435/7.92, 514/12, 530/300, 530/350, 536/23.5, 536/23.72, 930/220

APPL-NO: 8/ 555722
DATE FILED: November 14, 1995

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/273,059, entitled "E6 Binding Proteins" which was filed on Jul. 8, 1994, now abandoned, the specification of which are incorporated by reference herein .

IN: Androphy; Elliot J., Chen; Jason J.

AB: E6-BP polypeptides, nucleic acids encoding E6-BP polypeptides, and uses thereof.

12. Document ID: US 5981702 A

L3: Entry 12 of 58

File: USPT

Nov 9, 1999

US-PAT-NO: 5981702
DOCUMENT-IDENTIFIER: US 5981702 A
TITLE: Cyclin/CDK associated proteins, and uses related thereto
DATE-ISSUED: November 9, 1999

US-CL-CURRENT: 530/350

APPL-NO: 8/ 531439
DATE FILED: September 21, 1995

IN: Zhang; Hui, Beach; David

AB: The present invention relates to the discovery in mammalian cells, particularly human cells, of novel S-phase kinase associated proteins, p19 and p45, referred to herein as "Skp". As described herein, these proteins are components of the tumor cell-specific cyclin A/CDK2 complex and function to facilitate DNA replication. Interference with p45 function in vivo prevented entry into S-phase in both normal and transformed cells. Binding data indicated that p45 and p19 associate with each other in a binary complex. Moreover, p45 is required for p19 binding to cyclin A/CDK2.

13. Document ID: US 5968821 A

L3: Entry 13 of 58

File: USPT

Oct 19, 1999

US-PAT-NO: 5968821
DOCUMENT-IDENTIFIER: US 5968821 A
TITLE: Cell-cycle regulatory proteins, and uses related thereto
DATE-ISSUED: October 19, 1999

US-CL-CURRENT: 435/325; 435/320.1, 435/455, 435/6, 435/69.1, 536/23.1

APPL-NO: 8/ 893274
DATE FILED: July 15, 1997

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation application of Ser. No. 08/306,511 filed on Sep. 14, 1994, which is a continuation-in-part of U.S. Ser. No. 08/248,812 filed May 25, 1994 and entitled "Cell-cycle Regulatory Protein, and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 08/227,371 filed Apr. 14, 1994 and entitled "Cell-cycle Regulatory Protein, and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 08/154,915 filed Nov. 18, 1993 and entitled "Cyclin Complex Rearrangements and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 07/991,997 filed Dec. 17, 1992 and entitled "Cyclin Complex Rearrangements and Uses Related Thereto", abandoned, which is a continuation-in-part of U.S. Ser. No. 07/963,308 filed Oct. 16, 1992 and entitled "D-Type Cyclin and Uses Related Thereto". The teachings of U.S. Ser. Nos. 08/248,812, 08/227,371, 08/154,915, 07/991,997, 07/963,308 and related PCT publication US93/09945 are incorporated herein by reference.

IN: Beach; David H., Demetrick; Douglas J., Serrano; Manuel, Hannon; Gregory J.

AB: The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of a novel family of cell-cycle regulatory proteins ("CCR-proteins"). As described herein, this family of proteins includes a polypeptide having an apparent molecular weight of 16 kDa, and a polypeptide having an apparent molecular weight of approximately 15 kDa, each of which can function as an inhibitor of cell-cycle progression, and therefore ultimately of cell growth. Thus, similar to the role of p21 to the p53 checkpoint, the subject CCR-proteins may function coordinately with the cell-cycle regulatory protein, retinoblastoma (RB). Furthermore, the CCR-protein family includes a protein having an apparent molecular weight of 13.5 kDa (hereinafter "p13.5"). The presumptive role of p13.5, like p16 and p15, is in the regulation of the cell-cycle.

14. Document ID: US 5965790 A

L3: Entry 14 of 58

File: USPT

Oct 12, 1999

US-PAT-NO: 5965790
DOCUMENT-IDENTIFIER: US 5965790 A
TITLE: SR-BI regulatory sequences and therapeutic methods of use
DATE-ISSUED: October 12, 1999

US-CL-CURRENT: 800/18; 435/29, 435/320.1, 435/325, 435/6, 536/24.1, 536/24.31, 800/21

APPL-NO: 8/ 812204
DATE FILED: March 6, 1997

IN: Acton; Susan Laurene

AB: The invention features nucleic acid molecules that are involved with (e.g. activate or regulate) human SR-BI receptor transcription, as well as complements thereto, and homologs thereof. In addition, drug discovery assays are provided for identifying agents which modulate SR-BI promoter activity and thereby modulate the expression of a gene regulated thereby. Such agents can be useful therapeutically for treating or preventing the development of a disease or condition that is caused or contributed to by an aberrant SR-BI activity. In a preferred embodiment, the disease or condition is characterized by inappropriate lipid transfer or metabolism (e.g., atherosclerosis or gallstone formation). Such agents can also be used to modulate expression of a specific gene under the control of the SR-BI promoter in gene therapy. Moreover,.the present invention provides diagnostic assays and reagents for determining whether a subject has a disorder involving, for example, aberrant expression of SR-BI genes.

15. Document ID: US 5962316 A

L3: Entry 15 of 58

File: USPT

Oct 5, 1999

US-PAT-NO: 5962316
DOCUMENT-IDENTIFIER: US 5962316 A
TITLE: Cell-cycle regulatory proteins, and uses related thereto
DATE-ISSUED: October 5, 1999

US-CL-CURRENT: 435/325; 424/185.1, 424/93.21, 435/320.1, 435/455, 435/6, 435/69.1, 514/44, 530/350, 536/23.1, 536/23.4, 536/23.5, 536/24.1

APPL-NO: 8/ 306511
DATE FILED: September 14, 1994

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/248,812 filed May 25, 1994 and entitled "Cell-cycle Regulatory Protein, and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 08/227,371 filed Apr. 14, 1994 and entitled "Cell-cycle Regulatory Protein, and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 08/154,915 filed Nov. 18, 1993 and entitled "Cyclin Complex Rearrangements and Uses Related Thereto", which is a continuation-in-part of U.S. Ser. No. 07/991,997 filed Dec. 17, 1992 and entitled "Cyclin Complex Rearrangements and Uses Related Thereto", now abandoned, which is a continuation-in-part of U.S. Ser. No. 07/963,308 filed Oct. 16, 1992 and entitled "D-Type Cyclin and Uses Related Thereto". The teachings of U.S. Ser. Nos. 08/248,812, 08/227,371, 08/154,915, 07/991,997, 07/963,308 and related PCT publication US 93/09945 are incorporated herein by reference.

IN: Beach; David H., Demetrick; Douglas J., Serrano; Manuel, Hannon; Gregory J.

AB: The present invention relates to the discovery in eukaryotic cells, particularly mammalian cells, of a novel family of cell-cycle regulatory proteins ("CCR-proteins"). As described herein, this family of proteins includes a polypeptide having an apparent molecular weight of 16 kDa, and a polypeptide having an apparent molecular weight of approximately 15 kDa, each of which can function as an inhibitor of cell-cycle progression, and therefore ultimately of cell growth. Thus, similar to the role of p21 to the p53 checkpoint, the subject CCR-proteins may function coordinately with the cell-cycle regulatory protein, retinoblastoma (RB). Furthermore, the CCR-protein family includes a protein having an apparent molecular weight of 13.5 kDa (hereinafter "p13.5"). The presumptive role of p13.5, like p16 and p15, is in the regulation of the cell-cycle.

16. Document ID: US 5955306 A

L3: Entry 16 of 58

File: USPT

Sep 21, 1999

US-PAT-NO: 5955306
DOCUMENT-IDENTIFIER: US 5955306 A
TITLE: Genes encoding proteins that interact with the tub protein
DATE-ISSUED: September 21, 1999

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 435/71.1, 536/23.5, 536/24.3, 536/24.31

APPL-NO: 8/ 897340
DATE FILED: July 21, 1997

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/715,032, filed Sep. 17, 1996, now abandoned, the contents of which are incorporated herein by reference.

IN: Gimeno; Carlos J., Errada; Patrick R.

AB: The present invention relates to the discovery of novel genes encoding Tub interactor (TI) polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.

17. Document ID: US 5948653 A

L3: Entry 17 of 58

File: USPT

Sep 7, 1999

US-PAT-NO: 5948653
DOCUMENT-IDENTIFIER: US 5948653 A
TITLE: Sequence alterations using homologous recombination
DATE-ISSUED: September 7, 1999

US-CL-CURRENT: 435/6; 435/470, 435/471, 435/490, 435/91.1, 435/DIG.37, 435/DIG.5, 435/DIG.6, 435/DIG.8, 530/350, 536/23.1

APPL-NO: 8/ 910367
DATE FILED: August 13, 1997

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application claims the benefit of U.S. application Ser. No. 60/041,173, filed 21, Mar. 1997.

IN: Pati; Sushma, Zarling; David A.

AB: The invention relates to methods for targeting an exogenous polynucleotide or exogenous complementary polynucleotide pair to a predetermined endogenous DNA target sequence in a target cell by homologous pairing, particularly for altering an endogenous DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous recombination. In certain embodiments, the invention relates to methods for targeting an exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous DNA sequence in a metabolically active target cell, generating a DNA sequence-specific targeting of one or more chemical substituents in an intact nucleus of a metabolically active target cell, generally for purposes of altering a predetermined endogenous DNA sequence in the cell. The invention also relates to compositions that contain exogenous targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides, chemical substituents of such polynucleotides, and recombinase proteins used in the methods of the invention.

18. Document ID: US 5945339 A

L3: Entry 18 of 58

File: USPT

Aug 31, 1999

US-PAT-NO: 5945339
DOCUMENT-IDENTIFIER: US 5945339 A
TITLE: Methods to promote homologous recombination in eukaryotic cells and organisms
DATE-ISSUED: August 31, 1999

US-CL-CURRENT: 435/477; 435/483, 435/484

APPL-NO: 9/ 114637
DATE FILED: July 13, 1998

PARENT-CASE:
This application is a continuation of application Ser. No. 08/373,134, filed Jan. 17, 1995, now U.S. Pat. No. 5,780,296.

IN: Holloman; William K., Kmiec; Eric B.

AB: The invention concerns genes encoding recombinases that can be used to promote homologous recombination in eukaryotic cells. The application teaches methods by which a recombinase of one species can be used to isolate a homologous recombinase of a different species and methods to identify the isolated homologs. Recombinases from Ustilago maydis, Saccharomyces cerevisiae and humans are specifically included in the invention., The invention encompasses the method of producing an isolated recombinase protein in a prokaryotic cell and recovering the product in an active form. The invention also encompasses a genetically engineered gene which encodes a non-naturally occurring recombinase that causes a greater rate of recombination than does the naturally occurring recombinase. The invention further encompasses the use of recombinase proteins and of recombinase genes to promote homologous recombination, including recombination between a host cell genome and a chimeric oligonucleotide, i.e., an oligonucleotide having both RNA and DNA bases.

19. Document ID: US 5919997 A

L3: Entry 19 of 58

File: USPT

Jul 6, 1999

US-PAT-NO: 5919997
DOCUMENT-IDENTIFIER: US 5919997 A
TITLE: Transgenic mice having modified cell-cycle regulation
DATE-ISSUED: July 6, 1999

US-CL-CURRENT: 800/18; 424/9.2, 435/320.1, 435/325, 435/455, 435/463, 435/467, 435/91.2, 800/22, 800/25, 800/3

APPL-NO: 8/ 627610
DATE FILED: April 4, 1996

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/581,918 filed Jan. 2, 1996 which is a continuation-in-part of U.S. Ser. No. 08/497,214 filed Jun. 30, 1995, which is a continuation-in-part of U.S. Ser. No. 08/346,147 filed Nov. 29, 1994, which is a continuation-in-part of U.S. Ser. No. 08/306,511 filed Sep. 14, 1994, which is a continuation-in-part of U.S. Ser. No. 08/248,812 filed May 25, 1994, which is a continuation-in-part of U.S. Ser. No. 08/227,371 filed Apr. 14, 1994, which is a

continuation-in-part of U.S. Ser. No. 08/154,915 filed Nov. 18, 1993. The teachings of U.S. Ser.
Nos. 08/497,214, 08/346,147, 08/306,511, 08/248,812, 08/227,371 and 08/154,915 (hereinafter the
"priority documents") are incorporated herein by reference.

IN: Beach; David H., Serrano; Manuel, DePinho; Ronald A.

AB: The present invention relates to transgenic mice in which the biological function
of at least one cell cycle regulatory proteins of the INK4 family is altered.

20. Document ID: US 5912326 A

L3: Entry 20 of 58

File: USPT

Jun 15, 1999

US-PAT-NO: 5912326
DOCUMENT-IDENTIFIER: US 5912326 A
TITLE: Cerebellum-derived growth factors
DATE-ISSUED: June 15, 1999

US-CL-CURRENT: 530/399; 530/350

APPL-NO: 8/ 525864
DATE FILED: September 8, 1995

IN: Chang; Han

AB: The present invention relates to the discovery of a novel erbB receptor ligand,
referred to hereinafter as "cdGF", which protein has apparently broad involvement in the
formation and maintenance of ordered spatial arrangements of differentiated tissues in
vertebrates, and can be used to generate and/or maintain an array of different vertebrate
tissue both in vitro and in vivo.

21. Document ID: US 5910415 A

L3: Entry 21 of 58

File: USPT

Jun 8, 1999

US-PAT-NO: 5910415
DOCUMENT-IDENTIFIER: US 5910415 A
TITLE: Controlled modification of eukaryotic genomes
DATE-ISSUED: June 8, 1999

US-CL-CURRENT: 435/6; 435/320.1, 435/410, 536/23.1, 800/266, 800/267, 800/278

APPL-NO: 9/ 006232
DATE FILED: January 13, 1998

PARENT-CASE:
This is a Divisional of U.S. application Ser. No. 08/612,551 filed Mar. 8, 1996, now U.S. Pat.
No. 5,5744,336 which is a Divisional of U.S. application Ser. No. 08/010,997 filed Jan. 29, 1993,
now U.S. Pat. No. 5,527,695.

IN: Hodges; Thomas K., Lyznik; Leszek A.

AB: A method of using a unique DNA construct for the creation of transgenic
eukaryotic cells is described. The method allows a more precise and effective transformation
procedure that targets the insertion of a DNA sequence into a predetermined DNA locus, while
enabling the removal of any randomly inserted DNA sequences that occur as a by product of
known transformation procedures.

22. Document ID: US 5885776 A

L3: Entry 22 of 58

File: USPT

Mar 23, 1999

US-PAT-NO: 5885776
DOCUMENT-IDENTIFIER: US 5885776 A
TITLE: Glaucoma compositions and therapeutic and diagnositic uses therefor
DATE-ISSUED: March 23, 1999

US-CL-CURRENT: 435/6

APPL-NO: 8/ 791347
DATE FILED: January 30, 1997

IN: Stone; Edwin M., Sheffield; Val C., Alward; Wallace L. M.

AB: Methods and compositions for treating glaucoma; and glaucoma diagnostics are
disclosed.

23. Document ID: US 5882888 A

L3: Entry 23 of 58

File: USPT

Mar 16, 1999

US-PAT-NO: 5882888
DOCUMENT-IDENTIFIER: US 5882888 A
TITLE: DNA integration by transposition
DATE-ISSUED: March 16, 1999

US-CL-CURRENT: 435/69.1; 435/243, 435/252.31, 435/320.1, 435/473, 435/477, 435/478, 435/489,
435/91.4, 536/23.1, 536/24.2

APPL-NO: 8/ 875154
DATE FILED: July 17, 1997

FOREIGN-APPL-PRIORITY-DATA:
COUNTRY
APPL-NO

APPL-DATE
DK
0083/95
January 23, 1995
DK
0799/95
July 6, 1995

PCT-DATA:
APPL-NO
DATE-FILED
PUB-NO
PUB-DATE
371-DATE
102(E)-DATE
PCT/DK96/00038
Jan 23, 1996
WO96/23073
Aug 1, 1996
Jul 17, 1997
Jul 17, 1997

IN: J.o slashed.rgensen; Steen Troels

AB: Multicopy strains of gram-positive bacteria carrying multiple copies of a DNA
sequence of interest may be constructed by use of a method involving introduction of a DNA
construct comprising the DNA sequence of interest into the genome of the recipient cell by
transposition and subsequent deletion of a marker gene used for selection of the cells
having received the DNA construct by a resolution system. The multicopy strains are
preferably free from a gene encoding an undesirable marker such as an antibiotic resistance
marker.

24. Document ID: US 5874283 A

L3: Entry 24 of 58
File: USPT
Feb 23, 1999

US-PAT-NO: 5874283
DOCUMENT-IDENTIFIER: US 5874283 A
TITLE: Mammalian flap-specific endonuclease
DATE-ISSUED: February 23, 1999

US-CL-CURRENT: 435/252.3; 435/199, 435/252.33, 435/320.1, 435/69.1, 530/350, 536/23.2, 536/23.5

APPL-NO: 8/ 455968
DATE FILED: May 30, 1995

IN: Harrington; John Joseph, Hsieh; Chih-Lin, Lieber; Michael R.

AB: Compositions comprising human FEN-1(flap) endonucleases, nucleic acids encoding
them, and methods for their use are provided.

25. Document ID: US 5849989 A

L3: Entry 25 of 58
File: USPT
Dec 15, 1998

US-PAT-NO: 5849989
DOCUMENT-IDENTIFIER: US 5849989 A
TITLE: Insulin promoter factor, and uses related thereto
DATE-ISSUED: December 15, 1998

US-CL-CURRENT: 800/9; 800/18

APPL-NO: 8/ 320148
DATE FILED: October 7, 1994

IN: Edlund; Thomas

AB: The present invention relates to the discovery in eukaryotic cells, particularly
mammalian cells, of novel a transcriptional regulatory factor, referred to hereinafter as
"Insulin Promoter Factor 1" or "Ipf1".

26. Document ID: US 5844079 A

L3: Entry 26 of 58
File: USPT
Dec 1, 1998

US-PAT-NO: 5844079
DOCUMENT-IDENTIFIER: US 5844079 A
TITLE: Vertebrate embryonic pattern-inducing proteins, and uses related thereto
DATE-ISSUED: December 1, 1998

US-CL-CURRENT: 530/350; 435/252.3, 435/320.1, 435/69.1, 435/7.1, 530/300, 536/23.1, 536/23.5

APPL-NO: 8/ 356060
DATE FILED: December 14, 1994

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. Ser. No.
08/176,427 filed Dec. 30, 1993 and entitled "Vertebrate Embryonic Pattern-Inducing Proteins and
Uses Related Thereto", the teachings of which are incorporated herein by reference.

IN: Ingham; Philip W., McMahon; Andrew P., Tabin; Clifford J.

AB: The present invention concerns the discovery that proteins encoded by a family of
vertebrate genes, termed here hedgehog-related genes, comprise morphogenic signals produced
by embryonic patterning centers, and are involved in the formation of ordered spatial
arrangements of differentiated tissues in vertebrates. The present invention makes available
compositions and methods that can be utilized, for example to generate and/or maintain an
array of different vertebrate tissue both in vitro and in vivo.

27. Document ID: US 5834202 A

L3: Entry 27 of 58

File: USPT

Nov 10, 1998

US-PAT-NO: 5834202
DOCUMENT-IDENTIFIER: US 5834202 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: November 10, 1998

US-CL-CURRENT: 435/6; 435/320.1, 435/91.1, 435/91.2, 536/23.1, 536/24.2, 536/24.33

APPL-NO: 8/ 906491
DATE FILED: August 5, 1997

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent
application Ser. No. 08/595,226 (filed Feb. 1, 1996, which issued on Mar. 31, 1998, as U.S. Pat.
No. 5,733,733) which is a continuation-in-part of U.S. patent application Ser. No. 08/533,852
(filed Sep. 26, 1995, which issued on Mar. 25, 1997, as U.S. Pat. No. 5,614,389) which is a
continuation-in-part of U.S. patent application Ser. No. 08/383,327 (filed Feb. 3, 1995, which
issued on Jan. 7, 1997, as U.S. Pat. No. 5,591,609), which is a continuation-in-part of PCT
Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a continuation-in-part of U.S.
patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which application was abandoned in
favor of continuation application U.S. patent application Ser. No. 08/136,405, filed Oct. 15,
1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668), which is a continuation-in-part
of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992 (now abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and
in which the amplification is performed under isothermal conditions. The invention also
includes kits containing reagents for conducting the method.

28. Document ID: US 5830461 A

L3: Entry 28 of 58

File: USPT

Nov 3, 1998

US-PAT-NO: 5830461
DOCUMENT-IDENTIFIER: US 5830461 A
TITLE: Methods for promoting wound healing and treating transplant-associated vasculopathy
DATE-ISSUED: November 3, 1998

US-CL-CURRENT: 424/94.4; 424/94.1, 435/189

APPL-NO: 8/ 745375
DATE FILED: November 8, 1996

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent
application Ser. No. 08/630,798, filed Apr. 10, 1996, and which is a continuation-in-part of U.S.
patent application Ser. No. 08/265,046, filed Jun. 24, 1994, now U.S. Pat. No. 5,658,565, and a
continuation-in-part of U.S. patent application Ser. No. 08/465,522, filed Jun. 5, 1995, which is
a divisional of U.S. patent application Ser. No. 08/314,917, filed Sep. 28, 1994, now U.S. Pat.
No. 5,468,630, which is a continuation of U.S. patent application Ser. No. 07/981,344, filed Nov.
25, 1992, now abandoned.

IN: Billiar; Timothy R., Tzeng; Edith, Shears, II; Larry L., Geller; David A.,
Edington; Howard David James

AB: The present invention provides a method of promoting the closure of a wound in a
patient. This method involves transferring exogenous iNOS to the region of the wound whereby
a product of iNOS is produced in the region of the wound to promote the closure of the
wound.

29. Document ID: US 5807708 A

L3: Entry 29 of 58

File: USPT

Sep 15, 1998

US-PAT-NO: 5807708
DOCUMENT-IDENTIFIER: US 5807708 A
TITLE: Conservin nucleic acid molecules and compositions
DATE-ISSUED: September 15, 1998

US-CL-CURRENT: 435/69.1; 435/252.3, 435/254.11, 435/320.1, 435/325, 536/23.1, 536/23.5

APPL-NO: 8/ 688609
DATE FILED: July 30, 1996

IN: Falb; Dean A., Gimeno; Carlos J.

AB: The present invention relates to the discovery of novel conservin genes and
polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are
also disclosed.

30. Document ID: US 5800998 A

L3: Entry 30 of 58

File: USPT

Sep 1, 1998

US-PAT-NO: 5800998
DOCUMENT-IDENTIFIER: US 5800998 A
TITLE: Assays for diagnosing type II diabetes in a subject
DATE-ISSUED: September 1, 1998

US-CL-CURRENT: 435/6; 514/44, 536/23.1, 536/23.5

APPL-NO: 8/ 749431
DATE FILED: November 15, 1996

PARENT-CASE:
RELATED PATENT APPLICATIONS This patent application is a continuation-in-part (CIP) application
of U.S. Ser. No. 08/748,229 filed Nov. 2, 1996 (abandoned).

IN: Glucksmann; M. Alexandra

AB: Assays for determining whether a subject has or is at risk for developing type II
diabetes, which are based on detecting the presence or absence of alterations in the hepatic
nuclear factor 1 (HNF-1) gene or protein of the subject are disclosed.

31. Document ID: US 5795726 A

L3: Entry 31 of 58

File: USPT

Aug 18, 1998

US-PAT-NO: 5795726
DOCUMENT-IDENTIFIER: US 5795726 A
TITLE: Methods for identifying compounds useful in treating type II diabetes
DATE-ISSUED: August 18, 1998

US-CL-CURRENT: 435/7.21; 435/4, 435/6, 435/8, 536/23.5

APPL-NO: 8/ 782047
DATE FILED: January 10, 1997

PARENT-CASE:
RELATED PATENT APPLICATIONS The patent application is a continuation-in-part (CIP) application of
U.S. Ser. No. 08/760,246 filed Dec. 4, 1996, which itself is a CIP of U.S. Ser. No. 08/749,431
filed Nov. 15, 1996 which itself is a continuation-in-part of U.S. Ser. No. 08/748,229 filed Nov.
2, 1996 (abandoned).

IN: Glucksmann; M. Alexandra

AB: Methods for identifying compounds, which modulate the bioactivity of human
hepatic nuclear factor-1 (HNF-1), and which are therefore useful in treating type II
diabetes are disclosed.

32. Document ID: US 5795734 A

L3: Entry 32 of 58

File: USPT

Aug 18, 1998

US-PAT-NO: 5795734
DOCUMENT-IDENTIFIER: US 5795734 A
TITLE: EPH receptor ligands, and uses related thereto
DATE-ISSUED: August 18, 1998

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 435/7.1, 530/300, 530/350, 536/23.1,
536/23.5

APPL-NO: 8/ 455001
DATE FILED: May 31, 1995

PARENT-CASE:
REFERENCE TO RELATED APPLICATIONS This application in a continuation-in-part of U.S. Ser. No.
08/393,462, filed Feb. 27, 1995 and entitled "EPH Receptor Ligands, and Uses Related Thereto",
which is a continuation-in-part of U.S. Ser. No. 08/308,814, filed Sep. 19, 1994 and entitled
"EPH Receptor Ligands, and Uses Related Thereto". The disclosure of U.S. Ser. No. 08/308,814 and
08/393,462 are incorporated by reference.

IN: Flanagan; John G., Cheng; Hwai-Jong

AB: The present invention relates to the discovery of a novel EPH receptor ligand,
referred to hereinafter as "Elf-1", which protein has apparently broad involvement in the
formation and maintenance of ordered spatial arrangements of differentiated tissues in
vertebrates, and can be used to generate and/or maintain an array of different vertebrate
tissue both in vitro and in vivo.

33. Document ID: US 5792833 A

L3: Entry 33 of 58

File: USPT

Aug 11, 1998

US-PAT-NO: 5792833
DOCUMENT-IDENTIFIER: US 5792833 A
TITLE: E2 binding proteins
DATE-ISSUED: August 11, 1998

US-CL-CURRENT: 530/350; 530/300

APPL-NO: 8/ 361806
DATE FILED: December 22, 1994

IN: Androphy; Elliot J., Breiding; David E.

AB: E2-BP polypeptides, nucleic acids encoding E2-BP polypeptides, and uses thereof.

34. Document ID: US 5780296 A

L3: Entry 34 of 58

File: USPT

Jul 14, 1998

US-PAT-NO: 5780296
DOCUMENT-IDENTIFIER: US 5780296 A
TITLE: Compositions and methods to promote homologous recombination in eukaryotic cells and
organisms
DATE-ISSUED: July 14, 1998

US-CL-CURRENT: 435/320.1; 536/23.2

APPL-NO: 8/ 373134
DATE FILED: January 17, 1995

IN: Holloman; William K., Kmiec; Eric B.

AB: The invention concerns genes encoding recombinases that can be used to promote
homologous recombination in eukaryotic cells and expression vectors that can be used to
transiently express recombinases in target cells. One embodiment of the invention
encompasses genetically engineered nucleic acids that encode a non-naturally occurring
recombinase that causes a greater rate of recombination than does the naturally occurring
recombinase. Recombinases from Ustilago maydis, Saccharomyces cerevisiae are specifically
included in the invention.

35. Document ID: US 5770384 A

L3: Entry 35 of 58

File: USPT

Jun 23, 1998

US-PAT-NO: 5770384
DOCUMENT-IDENTIFIER: US 5770384 A
TITLE: Method for determining compound interaction with E2 binding proteins
DATE-ISSUED: June 23, 1998

US-CL-CURRENT: 435/7.8; 435/5, 435/69.1, 435/69.7, 435/7.1, 435/7.93, 514/2, 530/300, 530/350,
536/23.72

APPL-NO: 8/ 612986
DATE FILED: March 6, 1996

PARENT-CASE:
This application is a divisional application of U.S. Ser. No. 08/361,806 filed on Dec. 22, 1994,
pending. The contents of all of the aforementioned application are hereby incorporated by
reference.

IN: Androphy; Elliot J., Breiding; David E.

AB: E2-BP polypeptides, nucleic acids encoding E2-BP polypeptides, and uses thereof.

36. Document ID: US 5763240 A

L3: Entry 36 of 58

File: USPT

Jun 9, 1998

US-PAT-NO: 5763240
DOCUMENT-IDENTIFIER: US 5763240 A
TITLE: In vivo homologous sequence targeting in eukaryotic cells
DATE-ISSUED: June 9, 1998

US-CL-CURRENT: 435/463; 435/6, 435/91.1, 435/91.4

APPL-NO: 8/ 275916
DATE FILED: July 14, 1994

PARENT-CASE:
This is a continuation of application Ser. No. 07/873,438 filed 24 Apr. 1992 now abandoned.

IN: Zarling; David A., Sena; Elissa P.

AB: The invention relates to methods for targeting an exogenous polynucleotide or
exogenous complementary polynucleotide pair to a predetermined endogenous DNA target
sequence in a eukaryotic cell by homologous pairing, particularly for altering an endogenous
DNA sequence, such as a chromosomal DNA sequence, typically by targeted homologous
recombination. In certain embodiments, the invention relates to methods for targeting an
exogenous polynucleotide having a linked chemical substituent to a predetermined endogenous
DNA sequence in a metabolically active eukaryotic cell, generating a DNA sequence-specific
targeting of one or more chemical substituents in an intact nucleus of a metabolically
active eukaryotic cell, generally for purposes of altering a predetermined endogenous DNA
sequence in the cell. The invention also relates to compositions that contain exogenous
targeting polynucleotides, complementary pairs of exogenous targeting polynucleotides,
chemical substituents of such polynucleotides, and recombinase proteins used in the methods
of the invention.

37. Document ID: US 5756671 A

L3: Entry 37 of 58

File: USPT

May 26, 1998

US-PAT-NO: 5756671
DOCUMENT-IDENTIFIER: US 5756671 A
TITLE: CDC37 cell-cycle regulatory protein, and uses related thereto
DATE-ISSUED: May 26, 1998

US-CL-CURRENT: 530/350; 530/300

APPL-NO: 8/ 625209
DATE FILED: April 1, 1996

PARENT-CASE:
RELATED APPLICATIONS This application is a continuation-in-part of U.S. Ser. No. 08/466,679 filed

Jun. 6, 1995, now abandoned, entitled "Cdc37 Cell-Cycle Regulatory Protein and Uses Related
Thereto", which is a continuation-in-part of U.S. Ser. No. 08/253,155 filed Jun. 2, 1994, now
U.S. Pat. No. 5,651,147, entitled "CDK4 Binding Proteins". The teachings of both U.S. Ser. Nos.
08/253,155 and 08/466,679 now abandoned are incorporated herein by reference.

IN: Gyuris; Jeno, Lamphere; Lou, Draetta; Giulio

AB: The present invention relates to the discovery in mammalian cells, particularly
human cells, of a novel CDK-binding protein, referred to herein as "cdc37". As described
herein, this protein functions to facilitate activation and accordingly functions in the
modulation of cell-cycle progression, and therefore ultimately of cell growth and
differentiation. Moreover, binding data indicated that cdc37 may function coordinately with
other cell-cycle regulatory proteins, such as of cyclin-dependent kinases (CDKs), src, p53
and erk kinases.

38. Document ID: US 5744336 A

L3: Entry 38 of 58

File: USPT

Apr 28, 1998

US-PAT-NO: 5744336
DOCUMENT-IDENTIFIER: US 5744336 A
TITLE: DNA constructs for controlled transformation of eukaryotic cells
DATE-ISSUED: April 28, 1998

US-CL-CURRENT: 435/320.1; 536/23.1, 536/24.1, 536/24.2

APPL-NO: 8/ 612551
DATE FILED: March 8, 1996

PARENT-CASE:
This is a division of application Ser. No. 08/010,997, filed Jan. 29, 1993 now U.S. Pat. No.
5,527,695.

IN: Hodges; Thomas K., Lyznik; Leszek A.

AB: DNA constructs are provided for the creation of transgenic eukaryotic cells.
These DNA constructs allow a more precise and effective transformation procedure by enabling
the targeting of DNA sequences for insertion into a particular DNA locus, while enabling the
removal of any randomly inserted DNA sequences that occur as a by product of known
transformation procedures.

39. Document ID: US 5733733 A

L3: Entry 39 of 58

File: USPT

Mar 31, 1998

US-PAT-NO: 5733733
DOCUMENT-IDENTIFIER: US 5733733 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: March 31, 1998

US-CL-CURRENT: 435/6; 435/320.1, 435/5, 435/91.1, 435/91.2, 536/23.1, 536/24.3, 536/24.33

APPL-NO: 8/ 595226
DATE FILED: February 1, 1996

PARENT-CASE:
FIELD OF THE INVENTION The present invention is in the field of recombinant DNA technology. This
invention is directed to a process for amplifying a nucleic acid molecule, and to the molecules
employed and produced through this process. CROSS-REFERENCE TO RELATED APPLICATIONS This
application is a continuation-in-part of U.S. patent application Ser. No. 08/533,852 (filed Sep.
26, 1995, now U.S. Pat. No. 5,614,389) which is a continuation-in-part of U.S. patent application
Ser. No. 08/383,327 (filed Feb. 3, 1995) now U.S. Pat. No. 5,591,609, which is a
continuation-in-part of PCT Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a
continuation-in-part of U.S. patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which
application was abandoned in favor of continuation application U.S. patent application Ser. No.
08/136,405, filed Oct. 15, 1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668), which
is a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992 (now
abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and
in which the amplification is performed under isothermal conditions. The invention also
includes kits containing reagents for conducting the method.

40. Document ID: US 5635381 A

L3: Entry 40 of 58

File: USPT

Jun 3, 1997

US-PAT-NO: 5635381
DOCUMENT-IDENTIFIER: US 5635381 A
TITLE: Agrobacterium bacteria capable of site-specific recombination
DATE-ISSUED: June 3, 1997

US-CL-CURRENT: 800/294; 435/199, 435/252.2, 435/252.3, 435/320.1, 435/419, 435/477, 435/71.2,
536/23.72

APPL-NO: 8/ 290933
DATE FILED: January 20, 1995

FOREIGN-APPL-PRIORITY-DATA:
COUNTRY
APPL-NO

APPL-DATE
NL
922005582
February 26, 1992

PCT-DATA:
APPL-NO
DATE-FILED
PUB-NO
PUB-DATE
371-DATE
102(E)-DATE
PCT/EP93/00463
Feb 25, 1993
WO93/17116
Sep 2, 1993
Jan 20, 1995
Jan 20, 1995

IN: Hooykaas; Paul J. J., Mozo; Teresa

AB: The invention provides Agrobacterium strains capable of producing a cite-specific recombinase capable of effecting site-specific recombination of a first and a second recombination site in Agrobacterium strains, when present therein, comprising a structural DNA sequence encoding said recombinase and a DNA sequence capable of controlling expression in Agrobacterium strains. The invention also provides methods for using the strains to transform plant cells.

41. Document ID: US 5631237 A

L3: Entry 41 of 58
File: USPT
May 20, 1997

US-PAT-NO: 5631237
DOCUMENT-IDENTIFIER: US 5631237 A
TITLE: Method for producing in vivo delivery of therapeutic agents via liposomes
DATE-ISSUED: May 20, 1997

US-CL-CURRENT: 514/44; 264/4.1, 264/4.3, 264/4.6, 424/417, 424/450, 428/402.2

APPL-NO: 8/ 241372
DATE FILED: May 10, 1994

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of Ser. No. 07/995,022, filed Dec. 22, 1992 (now abandoned).

IN: Dzau; Victor J., Kaneda; Yasufumi

AB: Methods and compositions are provided for intracellular transfer of a wide variety of agents, by using Sendai virus comprising liposomes having various compositions in the liposome lumen. A preferred method for preparing the liposomes provides for enhanced levels of luminal concentrations, as well as incorporation of high molecular weight molecules. The method comprises fusing liposomes, where one liposome comprises the Sendai virus proteins and the other liposome comprises the luminal composition. The subject methods find particular application with intranuclear transfer of nucleic acids, more particularly with cells of the vasculature.

42. Document ID: US 5614389 A

L3: Entry 42 of 58
File: USPT
Mar 25, 1997

US-PAT-NO: 5614389
DOCUMENT-IDENTIFIER: US 5614389 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: March 25, 1997

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1

APPL-NO: 8/ 533852
DATE FILED: September 26, 1995

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of U.S. patent application Ser. No. 08/383,327 (filed Feb. 3, 1995), which is a continuation-in-part of PCT Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a continuation-in-part of U.S. patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which application was abandoned in favor of continuation application U.S. patent application Ser. No. 08/136,405, filed Oct. 15, 1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668, U.S. patent application Ser. No. 07/933,445, which is a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992 (now abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.

43. Document ID: US 5591609 A

L3: Entry 43 of 58
File: USPT
Jan 7, 1997

US-PAT-NO: 5591609
DOCUMENT-IDENTIFIER: US 5591609 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: January 7, 1997

US-CL-CURRENT: 435/91.2; 435/6, 435/91.1, 435/91.5

APPL-NO: 8/ 383327
DATE FILED: February 3, 1995

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation-in-part of PCT
Application No. PCT/US93/07309 (filed Aug. 4, 1993), which is a continuation-in-part of U.S.
patent application Ser. No. 07/933,945, filed Aug. 24, 1992 (which application was abandoned in
favor of continuation application U.S. patent application Ser. No. 08/136,405, filed Oct. 15,
1993, which issued on Oct. 11, 1994 as U.S. Pat. No. 5,354,668) and U.S. patent application Ser.
No. 07/933,945 is a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed
Aug. 4, 1992 (now abandoned).

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and
in which the amplification is performed under isothermal conditions. The invention also
includes kits containing reagents for conducting the method.

44. Document ID: US 5571688 A

L3: Entry 44 of 58
File: USPT
Nov 5, 1996

US-PAT-NO: 5571688
DOCUMENT-IDENTIFIER: US 5571688 A
TITLE: Method of detecting gene expression
DATE-ISSUED: November 5, 1996

US-CL-CURRENT: 435/29; 435/34, 435/6

APPL-NO: 8/ 396415
DATE FILED: February 27, 1995

PARENT-CASE:
CROSS-REFERENCE TO OTHER APPLICATIONS This patent application is a continuation-in-part of U.S.
patent application Ser. No. 08/127,905, filed Sep. 28, 1993, pending and entitled Selection of
Bacterial Genes Induced in Host Tissue which is a continuation-in-part of U.S. patent application
Ser. No. 08/058,299, filed May 6, 1993, now U.S. Pat. No. 5,434,065 and entitled In Vivo
Selection of Microbial Virulence Genes.

IN: Mekalanos; John J., Camilli; Andrew

AB: A reporter system relating to in vivo expression technology was devised to aid in
the identification and study of genes that display temporal or spatial patterns of
expression during infection of host tissues. The method of this invention comprises
constructing a strain or pool of strains of a microorganism which contains an artificial
cointegrate comprising a reporter gene flanked by direct repeats of sequences to which a
resolvase enzyme binds, thus catalyzing excision of the reporter gene, and further contains
a coding sequence under the control of a promoter sequence which encodes transcripts, the
expression of which are easily monitored in vitro and which result in a permanent genetic
change, excision of the reporter gene, that is heritable and easily detectable subsequent to
induction of the synthetic operon.

45. Document ID: US 5527695 A

L3: Entry 45 of 58
File: USPT
Jun 18, 1996

US-PAT-NO: 5527695
DOCUMENT-IDENTIFIER: US 5527695 A
TITLE: Controlled modification of eukaryotic genomes
DATE-ISSUED: June 18, 1996

US-CL-CURRENT: 800/291; 435/320.1

APPL-NO: 8/ 010997
DATE FILED: January 29, 1993

IN: Hodges; Thomas K., Lyznik; Leszek A.

AB: DNA constructs are provided for the creation of transgenic eukaryotic cells.
These DNA constructs allow a more precise and effective transformation procedure by enabling
the targeting of DNA sequences for insertion into a particular DNA locus, while enabling the
removal of any randomly inserted DNA sequences that occur as a by product of known
transformation procedures.

46. Document ID: US 5512452 A

L3: Entry 46 of 58
File: USPT
Apr 30, 1996

US-PAT-NO: 5512452
DOCUMENT-IDENTIFIER: US 5512452 A
TITLE: Selection of bacterial genes induced in host tissues
DATE-ISSUED: April 30, 1996

US-CL-CURRENT: 435/25; 435/6

APPL-NO: 8/ 127905
DATE FILED: September 28, 1993

PARENT-CASE:
CROSS-REFERENCE TO OTHER APPLICATIONS This patent application is a continuation-in-part of U.S.
patent application No. 08/058299, filed May 6, 1993, U.S. Pat. No. 5,434,065, and entitled In
Vivo Selection of Microbial Virulence Genes.

IN: Mekalanos; John J., Camilli; Andrew

AB: A reporter system relating to in vivo expression technology was devised to aid in the identification and study of genes that display temporal or spatial patterns of expression during infection of host tissues. The method of this invention comprises integrating a site-specific DNA recombinase expression vector, and a reporter gene that is permanently removable by the recombinase, by way of homologous recombination into a microorganism's chromosome and inducing the expression of a synthetic operon which encodes transcripts, the expression of which are easily monitored in vitro and which result in a permanent genetic change, excision of the reporter gene, that is heritable and easily detectable subsequent to induction of the synthetic operon.

47. Document ID: US 5354668 A

L3: Entry 47 of 58

File: USPT

Oct 11, 1994

US-PAT-NO: 5354668
DOCUMENT-IDENTIFIER: US 5354668 A
TITLE: Methods for the isothermal amplification of nucleic acid molecules
DATE-ISSUED: October 11, 1994

US-CL-CURRENT: 435/91.1; 435/6

APPL-NO: 8/ 136405
DATE FILED: October 15, 1993

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application is a continuation of U.S. patent application Ser. No. 07/933,945, filed Aug. 24, 1992, now abandoned, which application was a continuation-in-part of U.S. patent application Ser. No. 07/924,643, filed Aug. 4, 1992.

IN: Auerbach; Jeffrey I.

AB: Methods for amplifying a nucleic acid molecule which employs a single primer, and in which the amplification is performed under isothermal conditions. The invention also includes kits containing reagents for conducting the method.

48. Document ID: US 5102797 A

L3: Entry 48 of 58

File: USPT

Apr 7, 1992

US-PAT-NO: 5102797
DOCUMENT-IDENTIFIER: US 5102797 A
TITLE: Introduction of heterologous genes into bacteria using transposon flanked expression cassette and a binary vector system

DATE-ISSUED: April 7, 1992

US-CL-CURRENT: 435/473; 435/320.1

APPL-NO: 7/ 357492
DATE FILED: May 26, 1989

IN: Tucker; William T., Gutterson; Neal I.

AB: This invention relates to a new method for inserting heterologous genes into the genome of a bacteria using a combined plasmid. The combined plasmid provides a cis complementation of transposase genes and transposable elements. The method involves the homologous recombination of a carrier plasmid and a functions plasmid to form the combined plasmid. The carrier plasmid contains a transposable element which flanks a generic expression cassette. The functions plasmid comprises transposase genes which complement the transposable element on the carrier plasmid. The combined plasmid is then transferred to a recipient and the recipient is monitored for integration of the generic expression cassette into the genome. The combined plasmid is preferably created by an in vivo homologous recombination of the carrier and functions plasmids.

49. Document ID: JP 11225785 A

L3: Entry 49 of 58

File: JPAB

Aug 24, 1999

PUB-NO: JP411225785A
DOCUMENT-IDENTIFIER: JP 11225785 A
TITLE: OPTIMIZATION OF CELL FOR ENDOGENOUS GENE ACTIVATION

PUBN-DATE: August 24, 1999

INT-CL (IPC): C12N 15/09; C12N 5/10; C12Q 1/68

APPL-NO: JP10342234
APPL-DATE: December 1, 1998

IN: HONOLD, KONRAD, HOLTSCHKE, THOMAS, STERN, ANNE

AB: PROBLEM TO BE SOLVED: To optimize the expression of a nucleic acid in cells by transfecting cells with a vector comprising a heteroexpression control sequence or the like, positive selection marker gene, site-specific recombinase target sequence and sequence capable of homologous recombination, followed by culturing the resultant cells., SOLUTION: The expression of a nucleic acid sequence endogenous in eukaryocytes is optimized by the following procedure: cells are transfected with a 1st vector comprising a 1st heteroexpression control sequence and a sequence of a 1st amplification gene or the like, positive selection marker gene, at least two target sequences of a site-specific recombinase, adjacent to the above sequences, and such a DNA sequence

as to be adjacent to
the above sequences and homologous with the nucleic acid portion in the genome of the cells
so as to be capable of homologous recombination; the resulting transfected cells are
cultured under such conditions as to cause the homologous recombination of the above vector,
and the resulting cells are isolated., COPYRIGHT: (C)1999,JPO

50. Document ID: US 5780296 A

L3: Entry 50 of 58

File: EPAB

Jul 14, 1998

PUB-NO: US005780296A
DOCUMENT-IDENTIFIER: US 5780296 A
TITLE: Compositions and methods to promote homologous recombination in eukaryotic cells and
organisms

PUBN-DATE: July 14, 1998

INT-CL (IPC): C12N 15/63
EUR-CL (EPC): C12N009/00

APPL-NO: US37313495
APPL-DATE: January 17, 1995
PRIORITY-DATA: US37313495A (January 17, 1995)

IN: HOLLOMAN, WILLIAM K, KMIEC, ERIC B

AB: The invention concerns genes encoding recombinases that can be used to promote
homologous recombination in eukaryotic cells and expression vectors that can be used to
transiently express recombinases in target cells. One embodiment of the invention
encompasses genetically engineered nucleic acids that encode a non-naturally occurring
recombinase that causes a greater rate of recombination than does the naturally occurring
recombinase. Recombinases from Ustilago maydis, Saccharomyces cerevisiae are specifically
included in the invention.

51. Document ID: WO 9622364 A1

L3: Entry 51 of 58

File: EPAB

Jul 25, 1996

PUB-NO: WO009622364A1
DOCUMENT-IDENTIFIER: WO 9622364 A1
TITLE: COMPOSITIONS AND METHODS TO PROMOTE HOMOLOGOUS RECOMBINATION IN EUKARYOTIC CELLS AND ORGANISMS

PUBN-DATE: July 25, 1996

INT-CL (IPC): C12N 9/00; C12N 9/22
EUR-CL (EPC): C12N009/00

APPL-NO: US09600265
APPL-DATE: January 16, 1996
PRIORITY-DATA: US37313495A (January 17, 1995)

IN: HOLLOMAN, WILLIAM K, KMIEC, ERIC B

AB: The invention concerns genes encoding recombinases that can be used to promote
homologous recombination in eukaryotic cells. The application teaches methods by which a
recombinase of one species can be used to isolate a homologous recombinase of a different
species and methods to identify the isolated homologs. Recombinases from Ustilago maydis and
Saccharomyces cerevisiae are specifically included in the invention. The invention
encompasses the method of producing an isolated recombinase protein in a prokaryotic cell
and recovering the product in an active form. The invention also encompasses a genetically
engineered gene which encodes a non-naturally occurring recombinase that causes a greater
rate of recombination than does the naturally occurring recombinase. The invention further
encompasses the use of recombinase proteins and of recombinase genes to promote homologous
recombination, including recombination between a host cell genome and a chimeric
oligonucleotide, i.e., an oligonucleotide having both RNA and DNA bases.

52. Document ID: US 5512452 A

L3: Entry 52 of 58

File: EPAB

Apr 30, 1996

PUB-NO: US005512452A
DOCUMENT-IDENTIFIER: US 5512452 A
TITLE: Selection of bacterial genes induced in host tissues

PUBN-DATE: April 30, 1996

INT-CL (IPC): C12Q 1/02; C12N 15/00
EUR-CL (EPC): C07K014/255; C12N015/10, C12N015/52 , C12N015/62 , C12N015/90 , C12Q001/68

APPL-NO: US12790593
APPL-DATE: September 28, 1993
PRIORITY-DATA: US12790593A (September 28, 1993)

IN: MEKALANOS, JOHN J, CAMILLI, ANDREW

AB: A reporter system relating to in vivo expression technology was devised to aid in
the identification and study of genes that display temporal or spatial patterns of
expression during infection of host tissues. The method of this invention comprises
integrating a site-specific DNA recombinase expression vector, and a reporter gene that is
permanently removable by the recombinase, by way of homologous recombination into a
microorganism's chromosome and inducing the expression of a synthetic

operon which encodes
transcripts, the expression of which are easily monitored in vitro and which result in a
permanent genetic change, excision of the reporter gene, that is heritable and easily
detectable subsequent to induction of the synthetic operon.

53. Document ID: AU 9919135 A, WO 9937755 A2
L3: Entry 53 of 58
File: DWPI
Aug 9, 1999

DERWENT-ACC-NO: 1999-458689
DERWENT-WEEK: 200001
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TITLE: New compositions and methods for targeting sequence modifications in related family genes

PRIORITY-DATA:
1997US-0070734
December 11, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 9919135 A	August 9, 1999	N/A	000	C12N015/00
WO 9937755 A2	July 29, 1999	E	047	C12N015/00

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
AU 9919135A	December 11, 1998	1999AU-0019135	N/A
AU 9919135A	N/A	WO 9937755	Based on
WO 9937755A2	December 11, 1998	1998WO-US26498	N/A

INT-CL (IPC): C12N 15/00

IN: LEHMAN, C W, PATI, S, ZARLING, D, ZENG, H

AB: NOVELTY - A composition is new comprising at least one recombinase and at least
two single-stranded targeting polynucleotides (I) which are substantially complementary to
each other and each having a consensus homology clamp for a gene family i.e. a homology
motif tag (HMT)., DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
following:, (1) a method (A) for targeting a sequence modification in at least one member of
a consensus family of genes in a cell by homologous recombination. The method involves
introducing into at least one cell at least one recombinase and (I);, (2) a method (B) of
making a non-human organism with a targeted sequence modification in at least one member of
a gene family by introducing into a cell at least one recombinase and (I). The animal formed
has at least one modification in at least one member of a consensus family of genes;, (3) a
method (C) of isolating a member of a gene family comprising a protein consensus sequence.
The method involves:, (a) adding the recombinase and (I) to a complex mixture of nucleic
acids where the targeting polynucleotides comprise a purification tag; and, (b) isolating
the member using the purification tag; and, (4) a non-human organism containing a sequence
modification in an endogenous consensus functional domain of a gene member of a gene
family., USE - The composition is useful in kit form which include the composition as
libraries or pools of degenerate cssDNA probes along with other reagents such as recombinase
etc. The methods and compositions are used for inactivation of a gene family gene i.e.
exogenous targeting polynucleotides can be used to inactivate, decrease or alter the
biological activity of one or more genes in a cell (or transgenic nonhuman animal or plant).
This is useful in the generation of animal models of disease, or in the elucidation of gene
function and activity. Alternatively, the biological activity of the wild-type gene may be
either decreased or the wild-type activity altered to mimic disease states. This includes
genetic manipulation of non-coding gene sequences that affect the transcription of genes,
including promoter, repressors, enhancers and transcriptional activating sequences., The
compositions are useful in identifying new members of gene families which may be useful in
functional genomic studies as well as in identification of new drug targets. HMTs used in
homologous recombination methods can generate animals that have a wide variety of mutations
in a wide variety of related genes, potentially resulting in a wide variety of phenotypes
including those related to disease states. This may also be done on a cellular level to
identify genes involved in cellular phenotypes i.e. target identification., ADVANTAGE - This
invention provides compositions and methods for the evaluation and characterization of
individual and sets of genes in disease states., Traditionally, exogenous sequences
transferred into eukaryotic cells underwent homologous recombination with homologous
endogenous sequences only at very low frequencies. Hence they were recombined inefficiently
and large numbers of cells were needed to be transfected, selected and screened in order to
generate a correctly targeted homologous recombinant. Several proteins or purified extracts
having the property of promoting homologous recombination (recombinase activity) have
recently been identified and the frequency of homologous recombination is enhanced by the
presence of these recombinase activities. Such recent advances have resulted in techniques
allowing enhanced homologous recombination (EHR)., Relaxing the amount of sequence identity

needed for homologous recombination allows greater flexibility to target related genes for
creating transgenic animals and cells containing modifications in gene family consensus
sequences.

54. Document ID: EP 977771 A1, WO 9842727 A1, AU 9865620 A, US 5948653 A
L3: Entry 54 of 58
File: DWPI
Feb 9, 2000

DERWENT-ACC-NO: 1998-542274
DERWENT-WEEK: 200012
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TITLE: Modification of target polynucleotide sequences - by homologous recombination using
recombinase and at least 2 single stranded polynucleotides complementary to each other, used for,
e.g. correcting diseased alleles in cystic fibrosis

PRIORITY-DATA:
1997US-0910367
August 13, 1997
1997US-0041173
March 21, 1997

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 977771 A1	February 9, 2000	E	000	C07H021/04
WO 9842727 A1	October 1, 1998	E	136	C07H021/04
AU 9865620 A	October 20, 1998	N/A	000	C07H021/04
US 5948653 A	September 7, 1999	N/A	000	C07H021/04

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
EP 977771A1	March 16, 1998	1998EP-0911735	N/A
EP 977771A1	March 16, 1998	1998WO-US05223	N/A
EP 977771A1	N/A	WO 9842727	Based on
WO 9842727A1	March 16, 1998	1998WO-US05223	N/A
AU 9865620A	March 16, 1998	1998AU-0065620	N/A
AU 9865620A	N/A	WO 9842727	Based on
US 5948653A	March 21, 1997	1997US-0041173	Provisional
US 5948653A	August 13, 1997	1997US-0910367	N/A

INT-CL (IPC): C07H 21/04; C07K 14/00; C12N 15/00; C12P 19/34

IN: PATI, S, ZARLING, D A

AB: The following are claimed: (1) preparation of a targeted sequence modification
(TSM) in a preselected target DNA sequence in a eukaryotic zygote by homologous
recombination, comprising introducing into at least 1 eukaryotic zygote at least 1
recombinase and at least 2 single-stranded (ss) targeting polynucleotides (PNs) that are
complementary to each other, and each having a homology clamp (HC) corresponding to or is
complementary to a preselected target DNA sequence; (2) preparation of TSM in a preselected
target DNA sequence in a cell by homologous recombination which contains an insertion,
carried out as in (1), but where PNs also each have an internal HC; (3) a method for
targeting and altering, by homologous recombination, a pre-selected target NA sequence in an
extrachromosomal sequence (ExS) of a prokaryotic cell, comprising: (a) adding to the
extrachromosomal sequence materials as in (1); (b) removing the recombinase, and (c)
introducing the altered element into a prokaryotic cell; (4) a method of generating a pool
of variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to
ExS at least 1 recombinase and pairs of ss targeting PNS which are complementary to each
other and each comprising HC corresponding to or being complementary to a preselected target
NA sequence, the pairs comprising a library of mismatches between the targeting PN and the
target NA sequence, to form a library of altered ExS's; (5) a method of generating a
cellular library comprising variant NA sequences of a pre-selected target NA sequence,
comprising introducing into a population of target cells materials as in (4), and (6) a
method similar to (5) comprising: (a) adding to ExS materials as in (4), to form altered
ExS's; (b) as in (3b), and (c) introducing the altered sequences into a population of a
target cells to form the library of variant NA sequences., USE - The method of (1) may be
used for targeting and altering, by homologous recombination, a pre-selected target nucleic
acid (NA) sequence (claimed). The methods can provide for the efficient

and specific
modification of targeted PNs. The methods can be used, e.g. to target chemical substituents
in a sequence-specific manner in vivo, to correct or to generate genetic mutations in
endogenous DNA sequences by homologous recombination and/or gene conversion, to produce
homologously targeted transgenic organisms, including animals and plants at high efficiency,
and in other application, e.g. targeted drug delivery, based on in vivo homologous pairing.
The methods can be used for correcting disease alleles involved in producing human genetic
diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g.
neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53)
or acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B
virus (HBV) infection., The following are claimed: (1) preparation of a targeted sequence
modification (TSM) in a preselected target DNA sequence in a eukaryotic zygote by homologous
recombination, comprising introducing into at least 1 eukaryotic zygote at least 1
recombinase and at least 2 single-stranded (ss) targeting polynucleotides (PNs) that are
complementary to each other, and each having a homology clamp (HC) corresponding to or is
complementary to a preselected target DNA sequence; (2) preparation of TSM in a preselected
target DNA sequence in a cell by homologous recombination which contains an insertion,
carried out as in (1), but where PNs also each have an internal HC; (3) a method for
targeting and altering, by homologous recombination, a pre-selected target NA sequence in an
extrachromosomal sequence (ExS) of a prokaryotic cell, comprising: (a) adding to the
extrachromosomal sequence materials as in (1); (b) removing the recombinase, and (c)
introducing the altered element into a prokaryotic cell; (4) a method of generating a pool
of variant NA sequences of a pre-selected target NA sequence in ExS, comprising adding to
ExS at least 1 recombinase and pairs of ss targeting PNS which are complementary to each
other and each comprising HC corresponding to or being complementary to a preselected target
NA sequence, the pairs comprising a library of mismatches between the targeting PN and the
target NA sequence, to form a library of altered ExS's; (5) a method of generating a
cellular library comprising variant NA sequences of a pre-selected target NA sequence,
comprising introducing into a population of target cells materials as in (4), and (6) a
method similar to (5) comprising: (a) adding to ExS materials as in (4), to form altered
ExS's; (b) as in (3b), and (c) introducing the altered sequences into a population of a
target cells to form the library of variant NA sequences., USE - The method of (1) may be
used for targeting and altering, by homologous recombination, a pre-selected target nucleic
acid (NA) sequence (claimed). The methods can provide for the efficient and specific
modification of targeted PNs. The methods can be used, e.g. to target chemical substituents
in a sequence-specific manner in vivo, to correct or to generate genetic mutations in
endogenous DNA sequences by homologous recombination and/or gene conversion, to produce
homologously targeted transgenic organisms, including animals and plants at high efficiency,
and in other application, e.g. targeted drug delivery, based on in vivo homologous pairing.
The methods can be used for correcting disease alleles involved in producing human genetic
diseases, such as inherited genetic diseases (e.g. cystic fibrosis) and neoplasia (e.g.
neoplasms induced by somatic mutation of an oncogene or tumour suppressor gene, such as p53)
or acquired diseases, particularly parasitic or viral diseases, such as human hepatitis B
virus (HBV) infection.

55. Document ID: US 5945339 A, WO 9622364 A1, AU 9646960 A, US 5780296 A, EP 873402 A1
L3: Entry 55 of 58

File: DWPI

Aug 31, 1999

DERWENT-ACC-NO: 1996-354521
DERWENT-WEEK: 199942
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TITLE: Isolated recombinase enzyme and gene - obtd. from Ustilago maydis, used to promote homologous recombination in eukaryotic cells

PRIORITY-DATA:
1995US-0373134 January 17, 1995
1998US-0114637 July 13, 1998

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5945339 A	August 31, 1999	N/A	000	C12N015/64
WO 9622364 A1	July 25, 1996	E	071	C12N009/00
AU 9646960 A	August 7, 1996	N/A	000	C12N009/00
US 5780296 A	July 14, 1998	N/A	000	C12N015/63
EP 873402 A1	October 28, 1998	E	000	C12N009/00

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
US 5945339A	January 17, 1995		

1995US-0373134
Cont of
US 5945339A
July 13, 1998
1998US-0114637
N/A
US 5945339A
N/A
US 5780296
Cont of
WO 9622364A1
January 16, 1996
1996WO-US00265
N/A
AU 9646960A
January 16, 1996
1996AU-0046960
N/A
AU 9646960A
N/A
WO 9622364
Based on
US 5780296A
January 17, 1995
1995US-0373134
N/A
EP 873402A1
January 16, 1996
1996EP-0902629
N/A
EP 873402A1
January 16, 1996
1996WO-US00265
N/A
EP 873402A1
N/A
WO 9622364
Based on

INT-CL (IPC): C12N 9/00; C12N 9/22; C12N 15/63; C12N 15/64

IN: HOLLOMAN, W K, KMIEC, E B

AB: Novel isolated protein (A): (a) is an ATPase having an apparent mol.wt. by
SDS-PAGE of greater than 70 kD; (b) catalyses the formation of complementary or identical
strand pairings of polydeoxynucleic acids (PDAs); (c) promotes homologous recombination (HR)
in a eukaryote; and (d) has a sequence contg. the tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg
/Lys) (I), Xaa = any amino acid., USE - The prods. and methods can be used to promote HR in
cells for, e.g. making specific genetic alterations in cells to produce a recombinant
protein, introducing specific alterations in embryonic stem cells or ova to be used in the
construction of transgenic animals, modifying in vitro explanted tissue stem cells, e.g.
haematopoietic stem cells, which can then be continued in culture or reimplanted into a
non-human host to produce a specific prod. or reimplanted into a human subject in need of
gene therapy for a medical condition., Novel isolated protein (A): (a) is an ATPase having
an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the formation of
complementary or identical strand pairings of polydeoxynucleic acids (PDAs); (c) promotes
homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the tetrapeptide
(I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino acid., USE - The prods. and methods
can be used to promote HR in cells for, e.g. making specific genetic alterations in cells to
produce a recombinant protein, introducing specific alterations in embryonic stem cells or
ova to be used in the construction of transgenic animals, modifying in vitro explanted
tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in culture or
reimplanted into a non-human host to produce a specific prod. or reimplanted into a human
subject in need of gene therapy for a medical condition., Novel isolated protein (A): (a) is
an ATPase having an apparent mol.wt. by SDS-PAGE of greater than 70 kD; (b) catalyses the
formation of complementary or identical strand pairings of polydeoxynucleic acids (PDAs);
(c) promotes homologous recombination (HR) in a eukaryote; and (d) has a sequence contg. the
tetrapeptide (I): (Ser/Thr)-Pro-Xaa-(Arg /Lys) (I), Xaa = any amino acid., USE - The prods.
and methods can be used to promote HR in cells for, e.g. making specific genetic alterations
in cells to produce a recombinant protein, introducing specific alterations in embryonic stem
cells or ova to be used in the construction of transgenic animals, modifying in vitro
explanted tissue stem cells, e.g. haematopoietic stem cells, which can then be continued in
culture or reimplanted into a non-human host to produce a specific prod. or reimplanted into
a human subject in need of gene therapy for a medical condition.

56. Document ID: US 5910415 A, WO 9417176 A1, EP 686191 A1, US 5527695 A, US 5744336 A
L3: Entry 56 of 58
File: DWPI
Jun 8, 1999

DERWENT-ACC-NO: 1994-264090
DERWENT-WEEK: 199930
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TITLE: DNA constructs - for creating transgenic eukaryotic cells

PRIORITY-DATA:
1993US-0010997
January 29, 1993
1996US-0612551
March 8, 1996
1998US-0006232
January 13, 1998

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5910415 A	June 8, 1999	N/A	000	C12Q001/68
WO 9417176 A1	August 4, 1994	E	079	C12N005/00
EP 686191 A1	December 13, 1995	E	000	

C12N005/00
US 5527695 A
June 18, 1996
N/A
027
C12N015/00
US 5744336 A
April 28, 1998
N/A
028
C07H021/04

APPLICATION-DATA:
PUB-NO
APPL-DATE
APPL-NO
APPL-DESCRIPTOR
US 5910415A
January 29, 1993
1993US-0010997
Div ex
US 5910415A
March 8, 1996
1996US-0612551
Div ex
US 5910415A
January 13, 1998
1998US-0006232
N/A
US 5910415A
N/A
US 5527695
Div ex
US 5910415A
N/A
US 5744336
Div ex
WO 9417176A1
January 27, 1994
1994WO-US00927
N/A
EP 686191A1
January 27, 1994
1994EP-0907893
N/A
EP 686191A1
January 27, 1994
1994WO-US00927
N/A
EP 686191A1
N/A
WO 9417176
Based on
US 5527695A
January 29, 1993
1993US-0010997
N/A
US 5744336A
January 29, 1993
1993US-0010997
Div ex
US 5744336A
March 8, 1996
1996US-0612551
N/A
US 5744336A
N/A
US 5527695
Div ex

INT-CL (IPC): A01H 1/04; A01H 4/00; A01H 5/00; A01H 5/10; C07H 21/04; C12N 5/00; C12N 15/00; C12N 15/09; C12N 15/63; C12N 15/82; C12Q 1/68

IN: HODGES, T K, LYZNIK, L A

AB: The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell
comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable
marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and
(iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell
sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences;
(2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA
comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s
recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence
targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a
sequence of interest and excisable selection region and flanked by: (iii) a sequence
homologous to eukaryotic cell sequences, where the excisable selection region comprises a
gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of
recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene
expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s
recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells
comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable
marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a
DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1
polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell
sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences., Also
claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in
vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly
selecting for insertion of a DNA sequence of interest into a specific sequence of an
organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying
selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing
randomly inserted DNA constructs; (d) applying selection means to isolate cells having the
targeted DNA sequence integrated into the organism's DNA via a homologous recombination
event; (e) removing the excisable selection region; and (f) culturing the resultant cells to
regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of
inducing an inducible promoter., USE - (I) can be used to target a DNA sequence of interest
into a specific site of a host cell's DNA. (II) is useful for directly selecting for
insertion of a DNA sequence of interest into a specific sequence of an organism's DNA.
Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest,
utilising (I), (II) or (III)., A method for the production of fertile, transgenic plants
wherein the transgenic plant has a DNA sequence of interest integrated at a predetermined
DNA sequence of the plant, said method comprising the steps of, introducing into plant cells
a DNA construct comprising, a multifunctional DNA sequence flanked by a pair of directly
repeated site-specific recombination sequences,, said multifunctional DNA sequence
comprising a gene encoding a selectable marker, and a DNA sequence of interest,, wherein

said DNA sequence of interest is flanked by nucleotide sequences sharing homology to the predetermined nucleotide sequence present in the plant cell, and the selectable marker gene is operably linked to regulatory sequences capable of expressing the gene in the plant cell,, selecting for plant cells having said DNA construct integrated into the DNA of the plant cell,, eliminating randomly inserted DNA constructs through expression of a recombinase gene capable of initiating recombination at the site-specific recombinase sequences in the plant cells,, identifying cells having said DNA sequence of interest integrated into the plant's DNA via a homologous recombination event, and, culturing said identified cells to generate an entire plant., The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences., Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter., USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III)., The following are new: (1) a DNA construct (I) for transforming a eukaryotic cell comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; and (iii) a sequence of interest flanked by (iv) sequences homologous to eukaryotic cell sequences; and (b) a pair of directly repeating site-specific (s-s) recombination sequences; (2) a DNA construct (II) for inserting a DNA sequence of interest into eukaryotic cell DNA comprising a multifunctional DNA sequence comprising: (i) a gene encoding a 1st s-s recombinase capable of recognising 1st s-s recombination sequences; (ii) a DNA sequence targeted for inversion via homologous recombination into eukaryotic cell DNA, comprising a sequence of interest and excisable selection region and flanked by: (iii) a sequence homologous to eukaryotic cell sequences, where the excisable selection region comprises a gene encoding a selectable marker and a gene encoding a 2nd s-s recombinase capable of recognising a 2nd s-s recombination sequence, both genes capable of eukaryotic gene expression, and the excisable region is flanked by: (iv) a pair of directly repeating s-s recombination sequences; and (3) a DNA construct (III) for transforming eukaryotic cells comprising: (a) a multifunctional DNA sequence comprising: (i) a gene encoding a selectable marker operably linked to (ii) regulatory sequences for eukaryotic gene expression; (iii) a DNA sequence targeted for inversion into the eukaryotic cell having less than or equal to 1 polylinker region and flanked by: (iv) nucleotide sequences homologous to eukaryotic cell sequences; and (b) a flanking pair of directly-repeated s-s recombination sequences., Also claimed are: (4) a plant entity comprising a plant cell, seed or plant, produced from the in vitro introduction of an exogenous DNA fragment into a plant cell; (5) a method for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA comprising: (a) introducing (II) into an organism's cells; (b) applying selection means to isolate cells contg. (II) integrated into cellular DNA; (c) removing randomly inserted DNA constructs; (d) applying selection means to isolate cells having the targeted DNA sequence integrated into the organism's DNA via a homologous recombination event; (e) removing the excisable selection region; and (f) culturing the resultant cells to regenerate an entire organism; and (6) a kit contg. (III) and an inducer cpd. capable of inducing an inducible promoter., USE - (I) can be used to target a DNA sequence of interest into a specific site of a host cell's DNA. (II) is useful for directly selecting for insertion of a DNA sequence of interest into a specific sequence of an organism's DNA. Fertile, transgenic plants can be produced (claimed) contg. a DNA sequence of interest, utilising (I), (II) or (III).

57. Document ID: US 5763240 A, WO 9322443 A1, AU 9341156 A, JP 07506252 W, EP 672159 A1
L3: Entry 57 of 58

File: DWPI

Jun 9, 1998

DERWENT-ACC-NO: 1993-368802
DERWENT-WEEK: 199830
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TITLE: In vivo homologous sequence targeting in eukaryotic cells - using a targeting
polynucleotide and recombinase to deliver agents or alter genes

PRIORITY-DATA:
1992US-0939767
September 2, 1992
1992US-0873438
April 24, 1992
1994US-0275916
July 14, 1994

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5763240 A	June 9, 1998	N/A	000	C12N015/64
WO 9322443 A1	November 11, 1993	E	100	C12N015/90
AU 9341156 A	November 29, 1993	N/A	000	C12N015/90
JP 07506252 W	July 13, 1995	N/A	027	C12N015/09
EP 672159 A1	September 20, 1995	E	000	C12N015/90

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
US 5763240A	April 24, 1992	1992US-0873438	Cont of
US 5763240A	July 14, 1994	1994US-0275916	N/A
WO 9322443A1	April 23, 1993	1993WO-US03868	N/A
AU 9341156A	April 23, 1993	1993AU-0041156	N/A
AU 9341156A	N/A	WO 9322443	Based on
JP07506252W	April 23, 1993	1993JP-0519421	N/A
JP07506252W	April 23, 1993	1993WO-US03868	N/A
JP07506252W	N/A	WO 9322443	Based on
EP 672159A1	April 23, 1993	1993EP-0910780	N/A
EP 672159A1	April 23, 1993	1993WO-US03868	N/A
EP 672159A1	N/A	WO 9322443	Based on

INT-CL (IPC): A01K 67/027; A61K 48/00; C12N 5/10; C12N 15/09; C12N 15/64; C12N 15/90; C12P 19/34;
C12Q 1/68; G01N 33/68

IN: SENA, E P, ZARLING, D A

AB: A method is claimed for targeting and altering, by homologous recombinatio n, a
pre-selected target DNA sequence in a eukaryotic cell to make a targeted sequence
modification, comprising (a) introducing into at least one eukaryotic cell at least one
recombinase and at least one targeting polynucleotide having a homology clamp that
corresponds to or is complementary to a preselected target DNA sequence and (b) identifying
a eukaryotic cell having a targeted DNA sequence modification at a preselected target DNA
sequence. Also claimed are (A) a compsn. for producing a targeted modification of an
endogenous DNA sequence, comprising a targeting polynucleotide and a recombinase; (B) a
compsn. for producing a targeted sequence modification of a human disease allele; a
targeting polynucleotide contg. a corrected sequence a recombinase or an expression
polynucleotide that encodes and expresses a recombinase; (C) a kit for therapy, monitoring
or prophylaxis of a genetic disease comprising a recombinase and a targeting polynucleotide;
(D) a method for treating a disease of an animal harbouring a disease allele, comprising
administering a compsn. consisting of: (a) a recombinase or an expression polynucleotide
encoding a recombinase and (b) a targeting polynucleotide which produces a sequence
modification upon homologous recombination with the disease allele; (E) an animal comprising
an allele that has a sequence modification as in (D)., USE/ADVANTAGE - The method can be
used to target chemical substits. (e.g. drugs) in a sequence-specific manner in vivo, to
correct or to generate genetic mutations in endogenous DNA sequence by homologous
recombination and/or gene conversion or to produce homologously targeted transgenic animals

at high efficiency. In partic., the method can be used for correcting disease alleles
involved in human genetic diseases such as inherited genetic disease (e.g. cystic fibrosis)
and neoplasm for treating or preventing viral diseases, by HBV hepatitis., A method is
claimed for targeting and altering, by homologous recombinatio n, a pre-selected target DNA
sequence in a eukaryotic cell to make a targeted sequence modification, comprising (a)
introducing into at least one eukaryotic cell at least one recombinase and at least one
targeting polynucleotide having a homology clamp that corresponds to or is complementary to
a preselected target DNA sequence and (b) identifying a eukaryotic cell having a targeted
DNA sequence modification at a preselected target DNA sequence. Also claimed are (A) a
compsn. for producing a targeted modification of an endogenous DNA sequence, comprising a
targeting polynucleotide and a recombinase; (B) a compsn. for producing a targeted sequence
modification of a human disease allele; a targeting polynucleotide contg. a corrected
sequence a recombinase or an expression polynucleotide that encodes and expresses a
recombinase; (C) a kit for therapy, monitoring or prophylaxis of a genetic disease
comprising a recombinase and a targeting polynucleotide; (D) a method for treating a disease
of an animal harbouring a disease allele, comprising administering a compsn. consisting of:
(a) a recombinase or an expression polynucleotide encoding a recombinase and (b) a targeting
polynucleotide which produces a sequence modification upon homologous recombination with the
disease allele; (E) an animal comprising an allele that has a sequence modification as in
(D)., USE/ADVANTAGE - The method can be used to target chemical substits. (e.g. drugs) in a
sequence-specific manner in vivo, to correct or to generate genetic mutations in endogenous
DNA sequence by homologous recombination and/or gene conversion or to produce homologously
targeted transgenic animals at high efficiency. In partic., the method can be used for
correcting disease alleles involved in human genetic diseases such as inherited genetic
disease (e.g. cystic fibrosis) and neoplasm for treating or preventing viral diseases, by
HBV hepatitis.

58. Document ID: EP 542466 A2, AU 655512 B, AU 9228316 A, CA 2082577 A, EP 542466 A3, JP 05336977 A, NZ 245070 A, ZA 9208662 A

L3: Entry 58 of 58

File: DWPI

May 19, 1993

DERWENT-ACC-NO: 1993-160938
DERWENT-WEEK: 199320
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TITLE: Baculovirus transfer vector contg. locus of crossover PI sequence - as substrate for recombinase enzyme, provides efficient homologous recombination with recombinant virus, esp. for expression of polypeptide(s) for vaccines

PRIORITY-DATA:
1991GB-0023929
November 11, 1991

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 542466 A2	May 19, 1993	E	018	C12N015/86
AU 655512 B	December 22, 1994	N/A	000	C12N015/86
AU 9228316 A	May 13, 1993	N/A	000	C12N015/86
CA 2082577 A	May 12, 1993	N/A	000	C12N015/86
EP 542466 A3	October 6, 1993	N/A	000	C12N015/86
JP 05336977 A	December 21, 1993	N/A	015	C12N015/86
NZ 245070 A	November 25, 1994	N/A	000	C12N015/74
ZA 9208662 A	July 27, 1994	N/A	036	C12N000/00

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	APPL-DESCRIPTOR
EP 542466A2	November 4, 1992	1992EP-0310085	N/A
AU 655512B	November 10, 1992	1992AU-0028316	N/A
AU 655512B	N/A	AU 9228316	N/A
AU 9228316A	November 10, 1992	1992AU-0028316	N/A
CA 2082577A	November 10, 1992	1992CA-2082577	N/A
EP 542466A3			

November 4, 1992
1992EP-0310085
N/A
JP05336977A
November 10, 1992
1992JP-0300156
N/A
NZ 245070A
November 10, 1992
1992NZ-0245070
N/A
ZA 9208662A
November 10, 1992
1992ZA-0008662
N/A

INT-CL (IPC): A61K 39/00; A61K 39/12; C12N 0/00; C12N 5/10; C12N 7/01; C12N 15/64; C12N 15/74;
C12N 15/86; G01N 33/53

IN: GEWERT, D R, PEAKMAN, T C

AB: New baculovirus transfer vector contains a restriction site for insertion of a
DNA sequence (I) encoding a heterologous polypeptide (II); regulatory elements for
expression of (I) when inserted and a loXP (locus of crossolver PI) DNA sequence (III) to
act as substrate for the Cre (causes recombination) recombinase protein (N)., Also new are
(1) recombinant DNA (V) comprising this vector and (I); (2) a baculovirus contg. (III) as
substrate for (IV); (3) recombinant baculovirus prepd. by homologous recombination of the
virus (2) and (V); (4) insect cells transfected with the recombinant virus; (5) vaccines
contg. (II) prepd. by culturing the transfected insect cells; and (6) test kits for
detecting (II)-specific antibodies or (II) themselves., (III) is esp. of formula,
5'-CCTTAATATAACTTCGTATAP
TGTATGCTATACGAAGTTATTAGGTCG 3'-GGAATTATATTGA
AGCATATTACA
TACGATATGCTTCAATAATCCAGC, USE/ADVANTAGE - The transfected cells provide high level
expression of (II) which are useful in human or veterinary medicine; in vaccines and in
diagnostic assays. The transfer vector provides an efficient in vitro system for
constructing recombinant viruses which can be identified and isolated. Up to 50 million
recombinants can be produced from 1 microg plasmid DNA and up to 50% of viral progeny are
recombinants. If required inserted genes are easily recovered and reinserted, and
recombination efficiency is independent of gene size (which can be 10kb or larger).